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Patient-Reported Outcomes of Split-Thickness Skin Grafts for Floor of Mouth Cancer Reconstruction

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Keywords
Oral cavity cancer · Oral cavity reconstruction · Split-thickness skin graft · Quality of life · Functional outcomes

Abstract
Introduction: Patient-reported outcome measures (PROM) on quality of life (QOL) for early-stage floor of mouth carcinoma (FOM-CA) undergoing surgical resection and split-thickness skin graft (STSG) reconstruction have not been established. We have performed a cross-sectional QOL analysis of such patients to define functional postoperative outcomes. ***Methods:*** Patients with pathologic stage T1/T2 FOM-CA who underwent resection and STSG reconstruction at a tertiary academic cancer center reported outcomes with the University of Washington QOL (v4) questionnaire after at least 6 months since surgery. ***Results:*** Twenty-four out of 49 eligible patients completed questionnaires with a mean follow-up of 41 months (range: 6–88). Subsites of tumor involvement/resection included the following: (1) lateral FOM (L-FOM) (n = 17), (2) anterior FOM (A-FOM) (n = 4), and (3) alveolar ridge with FOM, all of whom underwent lateral marginal mandibulectomy (MM-FOM) (n = 3). All patients reported swallowing scores of 70 ("I cannot swallow certain solid foods") or better. Ninety-six percent (23/24) reported speech of 70 ("difficulty saying some words, but I can be understood over the phone") or better. A-FOM patients reported worse chewing than L-FOM patients (mean: 50.0 vs. 85.3; p = 0.01). All 4 A-FOM patients reported a low chewing score of 50 ("I can eat soft solids but cannot chew some foods"). Otherwise, there were no significant differences between subsite groups in swallowing, speech, or taste. ***Conclusion:*** STSG reconstructions for pathologic T1–T2 FOM-CA appear to result in acceptable PROM QOL outcomes with the exception of A-FOM tumors having worse chewing outcomes.

Introduction

For ablation defects of early-stage floor of mouth carcinoma (FOM-CA), reconstructive options include secondary intention, split-thickness skin graft (STSG), local/

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regional pedicled flaps, and microvascular free flaps (FFs), as opposed to primary closure that could lead to tongue tethering. With the increasing utilization of FFs as a common reconstructive method for oral cavity cancer defects, particularly for FOM-CA, STSGs are likely being used less and less for reconstruction. The outcomes of STSGs for FOM-CA defects are not well studied. Past studies of oral cavity reconstruction have measured the defect size, anatomic factors, recipient site sensation, donor site morbidity, oral competence, and subjective physician-generated evaluations of postoperative tongue tethering, mobility, and speech intelligibility [1–11]. Patient-reported outcome measures (PROM) on quality of life (QOL) are becoming more widely used for functional outcome studies. Detailed PROMs of STSG reconstructions of FOM-CA have not yet been assessed to our knowledge. Given that STSGs, in comparison to FF, are more simple and efficient to perform with less morbidity and a shorter hospitalization and recovery, understanding STSG outcomes is important [7, 12–14]. The clinicopathologic factors related to FOM STSG reconstruction QOL outcomes are also unclear. Given these gaps, we conducted a study of patient-reported QOL outcomes after STSG reconstruction of early clinical T-stage (cT1/T2) FOM-CA defects.

Materials and Methods

We recruited all living patients, at least 18 years old, with a history of pathologic T1–2 FOM-CA who had undergone FOM resection with possible partial glossectomy and/or marginal mandibulectomy (MM) and reconstruction with a thigh STSG at the University of California, San Francisco (UCSF) Medical Center from August 2011 to October 2018 with at least 6 months of follow-up since surgery alone or completion of adjuvant radiation. We excluded patients with prior treatment, those who subsequently experienced locally recurrent disease, pathologic T3 and T4 tumors, and patients who underwent a near total or total glossectomy.

Patients were asked to complete the University of Washington Quality of Life (UW-QOL) Questionnaire version 4 in clinic or via email or mail [15, 16]. We assessed the outcomes from the 12 specific symptom domains (questions 1–12) in the questionnaire including pain, appearance, activity, recreation, swallowing, chewing, speech, shoulder, taste, saliva, mood, and anxiety. Each question is scored from 0 to 100 with a high score representing a high/healthy level of functioning. Demographic and clinicopathologic characteristics, and clinical outcomes were extracted during a retrospective review of operative and clinical notes, as well as imaging pathology reports. However, the following pertinent variables were not included in the results due to the inconsistent reporting of such information in the operative or pathology reports: status of lingual nerve during resection, total volume of tongue/FOM resection, and pathologic tumor depth of invasion, compared the patient study sample QOL responses with normative data previously published from a general dental practice population (n = 349) [17]. We also compared the study sample outcomes to a previously published QOL outcomes of a cohort of 36 patients having undergone partial glossectomy with reconstruction by various methods [18]. For analyses, patients were also categorized into an early follow-up group (completion of surveys between 6 and 12 months posttreatment) and a late follow-up group (completion of surveys >12 months posttreatment).

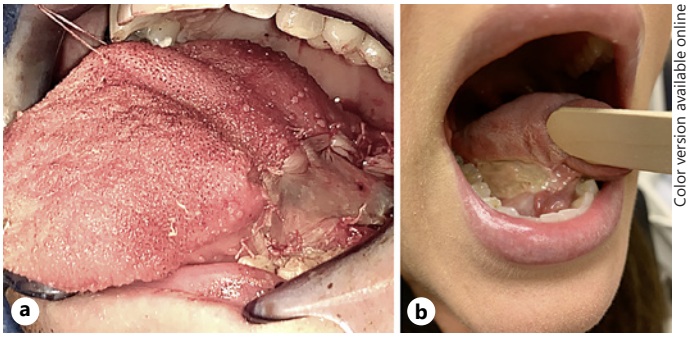

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Fig. 1. STSG reconstruction of lateral tongue and FOM. Representative photo intraoperatively following STSG inset (**a**) and postoperatively with characteristic well-healed appearance at 15 weeks after surgery (**b**). Note: photos are not taken from the same patient. STSG, split-thickness skin graft.

STSG FOM reconstructions were performed as previously described utilizing a dermatome with a depth of 0.015–0.020 inches (median 0.018) harvested from either the anterior thigh or the inguinal region [19–21]. In all cases, at the time of the ablation, a xeroform bolster was sutured over the STSG in the FOM and then removed at 5–7 days postoperatively (Fig. 1). The donor site from the STSG from the inguinal region is excised in an elliptical fashion and closed primarily for a cosmetically favorable linear incision in the inguinal crease (Fig. 2).

QOL responses were compared with a two-tailed Student's t test between domains of interest using a predefined alpha value of 0.05 defining statistical significance. A two-sample z test was utilized (α 0.04, standardized effect size 0.3) to compare generated QOL data with the previously published average normative data of the cohort of patients who underwent reconstruction by various methods [17, 18]. Statistical analyses were performed using RStudio version 1.1.442.

Results

Twenty-four out of 49 (49%) recruited alive patients completed questionnaires. There were 3 patient subsets based on tumor resection location: (1) lateral FOM (L-FOM) (n = 17), (2) anterior FOM (A-FOM) (n = 4), and (3) alveolar ridge with FOM, all of whom underwent a lateral MM (MM-FOM) (n = 3). There were no A-FOM or L-FOM patients who also underwent a MM. The ana-

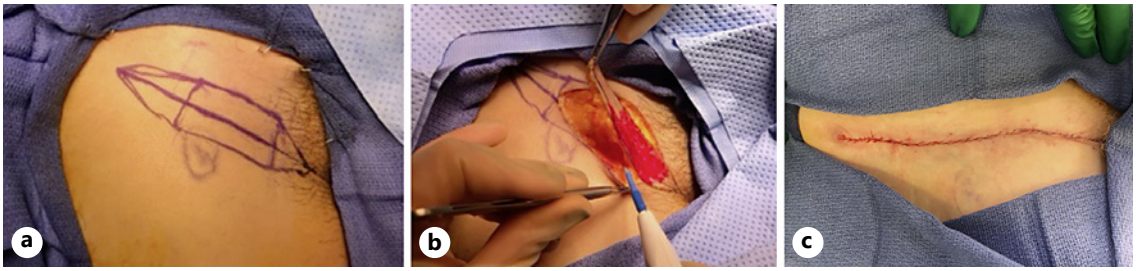

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Fig. 2. Elliptical excision and primary closure of inguinal STSG site. Intraoperative photos of STSG harvest site along the inguinal line (**a**), elliptical excision of STSG donor site (**b**), and primary closure of the donor site (**c**). STSG, split-thickness skin graft.

Table 1. Demographics and disease features

	All, *n* (%)	L-FOM	A-FOM	Alveolar ridge and FOM
N	24 (100)	17 (71)	4 (17)	3 (13)
Age, mean	66.8	65.7	65.8	74.3
Female sex	8 (33)	11 (65)	2 (50)	0 (0)
Follow-up, mean (range), months	41.1 (6–88)	39.2	32.5	63.7
Early follow-up (6–12 months)	4 (17)	3 (18)	1 (25)	0 (0)
Pathologic T stage				
T1	18 (75)	12 (71)	3 (75)	3 (100)
T2	6 (25)	5 (29)	1 (25)	0 (0)
Pathologic N Stage				
N0	12 (50)	8 (47)	3 (75)	1 (33)
N1	3 (13)	2 (12)	0	1 (33)
N2a	0	0	0	0
N2b	4 (17)	2 (12)	1 (25)	1 (33)
N2c	0	0	0	0
Not assessed (no neck dissection)	5 (21)	5 (29)	0	0
Pathologic tumor diameter, mean (min–max), cm	1.7 (0.1–4)	1.9 (0.6–4)	1.5 (0.7–3)	0.77 (0.1–1.1)
Adjuvant XRT	8 (33)	5 (29)	1 (25)	2 (66)

L-FOM, lateral FOM; A-FOM, anterior FOM.

tomic categories were determined upon surgeon description of subsite involvement/resection in the original operative report, with the mandibular canine defining the border between the A-FOM and L-FOM.

Table 1 describes patient, tumor, and treatment factors of the cohort. Response times ranged between 6 and 88 months after completion of treatment, with an average response time of 41 months. Among these, a majority (20/24) fell into the category of late follow-up defined by survey completion >12 months posttreatment. There was no significant difference between the average response time of L-FOM and A-FOM (39.2 vs. 32.5 months; p = 0.65), L-FOM and MM-FOM (39.2 vs. 63.7, p = 0.10), and A-FOM and MM-FOM (32.5 vs. 63.7 months, p = 0.24) patients. None of the patients in the cohort were edentulous. In addition, no postoperative surgical complications were reported in the clinical charts among our patient cohort, specifically including bleeding/hematoma, seroma, orocutaneous fistula, surgical site infection, donor site complications, or need for return to the operating room. One skin graft had a partial loss although there were no complete skin graft losses reported.

Table 2 shows the comparison of our study patient cohort, the normative patient cohort, and the Kazi et al. [18] cohort. In comparison with the normative patient cohort, on average our patient cohort reported significantly

Table 2. QOL outcomes

UW-QOL symptom domain	All STSG patients, $n = 24$, avg. (SD)	Published glossectomy cohort (Kazi et al. [18]), $n = 34$, avg. (SD); p value*	General population sample (Rogers [17]), $n = 349$, avg. (SD); p value*
Pain	85 (25)	85.3 (19.6); 0.99	86 (29); 0.92
Appearance	80 (20)	75.7 (18.9); 0.38	**92 (16); <0.01**
Activity	79 (26)	77.2 (19.8); 0.74	86 (21); 0.18
Recreation	81 (22)	79.4 (22.6); 0.75	86 (20); 0.24
Swallowing	87.5(15.1)	**75.6 (23.6); 0.03**	**98 (10); <0.01**
Chewing	79.2 (25.2)	67.6 (32.3); 0.15	**94 (17); <0.01**
Speech	72.1 (13.5)	79.8 (19.9); 0.11	**98 (12); <0.01**
Shoulder	78.6 (29.3)	65.7 (30.2); 0.11	**91 (22); 0.01**
Taste	70.0 (27.0)	72.8 (25.6); 0.69	**95 (14); <0.01**
Saliva	66.5 (33.0)	52.4 (27.9); 0.08	**97 (12); <0.01**
Mood	81.3 (21.2)	73.5 (22.9); 0.19	82 (23); 0.84
Anxiety	76.3 (22.8)	77.6 (19.6); 0.82	83 (26); 0.20

UW-QOL, University of Washington Quality of Life; STSG, split-thickness skin graft. * p values calculated relative to all STSG patients ($n = 24$). Bold values indicated statistical significance where $p < 0.05$.

worse outcomes in appearance, swallowing, chewing, speech, taste, and saliva. Relative to the outcomes data on partial glossectomy patients by Kazi et al. [18] (of which cohort 65% [$n = 22$] of the patients underwent adjuvant radiation), our study sample reconstructed with STSG reported significantly better swallowing but not significant differences in chewing, speech, and saliva.

Comparative QOL outcomes according to disease subsite (L-FOM, A-FOM, and MM-FOM), relative to normative population values, are shown in Figure 3. A-FOM patients reported statistically significantly worse chewing than L-FOM patients (mean: 50.0 vs. 85.3, respectively; $p = 0.01$). All 4 of the A-FOM patients each reported a chewing score of 50 that corresponds to an answer of "I can eat soft solids but cannot chew some foods." There were no other significant differences reported by patients between the 3 subsite groups in swallowing, speech, taste, or saliva.

The 8 (33%) patients in the study cohort who underwent adjuvant XRT reported significantly worse appearance (mean 62.5 vs. 89.0, respectively; $p < 0.01$). Otherwise, there was no significant difference between reported outcomes in swallowing, chewing, speech, and all other reported symptom domains (Table 3). There was no difference in average follow-up times between nonirradiated and radiated patients: mean 37.3 versus 48.9 months, respectively ($p = 0.31$).

Among all patients in the study, 19 (79%) also underwent neck dissection, while only 5 patients (21%) did not undergo neck dissection. There were no significant differences in reported outcomes between patients who underwent neck dissections compared to patients who did not, in swallowing (mean 85.8 vs. 94.0, respectively; $p = 0.29$), speech (mean 69.5 vs. 82.0, respectively; $p = 0.06$), chewing (mean 76.3 vs. 90.0, respectively; $p = 0.29$), or appearance (mean 80.3 vs. 80.0, respectively; $p = 0.98$).

Patients with early follow-up (6–12 months; $n = 4$) versus late follow-up (12+ months; $n = 20$) were compared. There was no difference in reported swallowing between early versus late follow-up, respectively, for swallowing (mean 100.0 vs. 85.0, $p = 0.07$) with all early follow-up patients reporting the highest score in swallowing (100), chewing (mean 87.5 vs. 77.5, $p = 0.48$), speech (mean 70.0 vs. 72.5, $p = 0.74$), taste (mean 85.0 vs. 67.0, $p = 0.23$), or saliva (mean 85.0 vs. 62.6, $p = 0.23$).

L-FOM patients with late follow-up who did not undergo adjuvant radiation ($n = 9$) were specifically analyzed and compared to the remainder of the patients in our cohort ($n = 15$), the Kazi et al. [18] glossectomy cohort, and the general normative population sample. When comparing the L-FOM non-XRT late-follow-up cohort to the remaining patients in our study population, there were no differences in swallowing (mean 86.7 vs. 88.0, $p = 0.84$), chewing (mean 83.3 vs. 76.8, $p = 0.54$), or speech (mean 76.7 vs. 69.3, $p = 0.20$), respectively. In comparison to the normative general dental population, the nonirradiated L-FOM cohort with late-follow-up group reported worse swallowing (mean 86.7 vs. 98.0, $p < 0.01$) and speech (mean 76.7 vs. 98.0, $p < 0.01$) but not

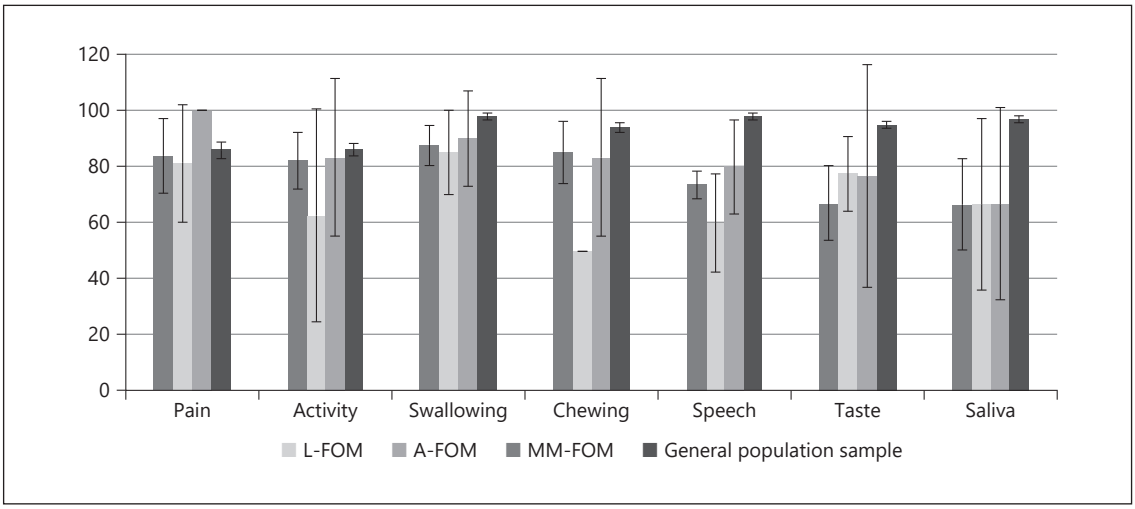

Fig. 3. QOL outcomes according to subsite. Three oral cavity subsites reconstructed with STSG in this study cohort including L-FOM, A-FOM, and MM-FOM are compared by QOL symptom categories, relative to normative population data published by Rogers et al. [17]. Error bars indicate 95% confidence interval. QOL, quality of life; STSG, split-thickness skin graft; L-FOM, lateral FOM; A-FOM, anterior FOM.

chewing (mean 83.3 vs. 94.0, $p = 0.07$), respectively. In comparison to the Kazi et al. [18] postglossectomy patients, there were no differences in swallowing (mean 86.7 vs. 75.6, $p = 0.19$), chewing (mean 83.3 vs. 67.6, $p = 0.18$), or speech (mean 76.7 vs. 79.8, $p = 0.66$), respectively.

The low number of possible outcomes scores in each symptom category prohibited a lowest-quartile analysis of the symptom categories of swallowing, chewing, and speech (e.g., the only possible chewing scores are 0, 50, and 100). We did evaluate the lowest-scoring patients in each category. There was only 1 patient reporting a speech score of 30 ("only my family and friends can understand me"), who had a pT2 tumor of A-FOM without adjuvant radiation. The remaining 23 (96%) patients reported speech of 70 ("I have difficulty saying some words, but I can be understood over the phone") or better. Forty-two percent (10/24) of patients reported a chewing score of 50 ("I can eat soft solids but cannot chew some foods") while 58% of patients reported a chewing score of 100 ("I can chew as well as ever"). The patients scoring 50 in chewing were over-represented by A-FOM subsite (all 4 A-FOM patients reported scores of 50), while 4 of the patients scoring 50 (40%) had undergone adjuvant radiation. None of the patients in our cohort reported swallowing <70 ("I cannot swallow certain solid foods"). Forty-two percent (10/24) of patients reported a swallowing score of 70, while the remainder reported a score of 100 ("I can swallow as well as ever").

Table 3. QOL outcomes by adjuvant radiation

UW-QOL symptom domain	No XRT, $n = 16$, avg. (SD)	XRT, $n = 8$, avg. (SD)	p value
Pain	86 (27)	84 (23)	0.89
Appearance	**89 (16)**	**63 (13)**	**<0.01**
Activity	77 (30)	84 (19)	0.50
Swallowing	89 (15)	85 (16)	0.58
Chewing	81 (25)	75 (27)	0.58
Speech	71 (15)	74 (11)	0.68
Taste	76 (23)	58 (32)	0.11
Saliva	73 (30)	54 (37)	0.18
Mood	81 (23)	81 (18)	1.00
Anxiety	74 (22)	80 (25)	0.58

QOL, Quality of Life; UW-QOL, University of Washington Quality of Life. Values in bold indicate statistical significance at $p < 0.05$.

Discussion

This is the first study, to our knowledge, to provide an in-depth analysis of PROMs of STSG for T1–2 FOM-CA defects according to disease- and treatment-specific factors, including anatomic subsite, postoperative adjuvant radiation, and follow-up time. STSG is an efficient reconstructive option for FOM-CA defects with low donor site

morbidity that can potentially lower operative time, hospital length of stay, and overall cost of care compared to FFs and pedicled myocutaneous flaps [22, 23]. In light of these advantages of this reconstructive method, understanding functional outcomes for STSG reconstruction of FOM-CA defects in the form of PROMs is important.

Overall, irrespective of FOM subsite and adjuvant radiation, most patients in this study reported acceptable results in swallowing and speech. A majority of patients reported totally normal swallowing with all patients reporting at least near normal swallowing. There was only 1 negative outlier in the speech symptom category (an A-FOM patient without adjuvant radiation). And, while a majority of STSG patients did in fact report normal swallowing, on average they nevertheless reported worse performance in chewing, swallowing, speech, and saliva than a normative population sample.

However, in order to contextualize STSG outcomes and understand their functionality relative to other oral cavity cancer patients, we compared their outcomes to a previously published cohort of partial glossectomy patients reconstructed by various methods (not including STSG) [18]. This reference cohort was chosen as a population more appropriate for comparison because it is a collection of exclusively oral cavity cancer cases without segmental mandibulectomy without other head and neck cancer subsites analyzed [24–26]. Swallowing was reported to be better in the study sample STSG patients than the Kazi et al. [18] cohort. Otherwise, outcomes in other oral domains were not significantly different [18]. These data do not allow direct comparison of QOL between reconstructive groups because the UW-QOL scores in Kazi et al. [18] were not reported according to reconstructive method. However, this comparison contextualizes the outcomes of our STSG patients. We infer from our data and the comparison that STSG for T1–T2 FOM-CA appears to be a reasonable reconstructive option from a QOL perspective with outcomes on par if not better than a more general cohort of partial glossectomy patients.

Our data suggest that A-FOM may be less appropriate for STSG reconstruction than other subsites, given that chewing was reported to be worse than L-FOM defects. Pedicled flap or FF reconstruction could possibly result in better chewing; however, no comparison has been performed for this scenario to our knowledge. It is not clear if a pedicled flap or FF would result in better or worse scores. This question would be an interesting area of comparison for future QOL studies. Regardless, this is the first report of baseline QOL outcomes for STSG reconstruction according to FOM subsites.

Based on empiric clinical observations, we hypothesized that the L-FOM nonirradiated patients would be a subset whose oral cavity function would be particularly high functioning. Despite our expectations, the 9 L-FOM patients with late follow-up (12+ months) and without adjuvant radiation reported functioning no better than the remaining patients in our study and did report worse swallowing and speech scores than the general normative population sample. Surprisingly, there were also no differences in swallowing, chewing, speech, taste, and saliva between patients having undergone adjuvant XRT and those who did not; however, this may be due to the small subset sample sizes.

Furthermore, while the difference in swallowing outcomes between early (6–12 months) and late (>12 months) follow-up approached but did not reach statistical significance, we suspect that a larger study cohort with a multivariate analysis may indeed reveal a real difference in this outcome. In a similar vein, the trends toward worse swallowing, speech, and chewing for those having undergone neck dissection relative to those who did not undergo neck dissection may also prove to be statistically significant with a larger study population with a multivariate analysis.

There were no complete STSG losses in our cohort, consistent with prior reports of excellent graft take intraorally following STSG [12, 14, 20]. In an aesthetically concerned patient, the cosmetic appearance of the STSG donor site can be minimized by full-thickness excision and closure of the STSG site following harvest either in the thigh or even along the inguinal line to hide it in the underwear or bathing suit line.

Ideally, QOL outcomes data will be used to directly compare reconstructive methods when controlling for tumor stage, subsite, radiation, and preoperative function in order to inform the head and neck surgeon's reconstructive algorithm for oral cavity defects. However, given that existing QOL studies on oral cavity cancer have traditionally focused on higher-stage tumors, FF reconstruction alone, or have not stratified data by tumor stage/subsite, future larger scale prospective studies with matched tumor cohorts will be necessary to better delineate QOL differences between STSG, pedicled flaps, and FFs in early stage tumors. This type of analysis has been performed comparing locoregional rotational flaps and FFs but not STSGs [18, 24, 27–32].

We acknowledge the limitations of this study. The low questionnaire response rate and low number of study subjects limited statistical comparisons and meaningful multivariate analyses. We did not have data on preoperative functional status or preoperative UW-QOL scores to al-

low for change of function analyses. FOM reconstruction and oral cavity reconstructive decision-making is inherently complex due to specific anatomic and size factors unique to each ablative defect and a surgeon's comfort and experience with certain methods. Specifically, other possible important factors that are not assessed in our study include the volume of ablative defect, anatomic details including degree of FOM resection and subsites of tongue resection, area of insensate tissue, and postoperative radiation dose and fields. The presence or absence of lingual nerve sacrifice was not uniformly recorded in operative reports or in follow up; as such, these incomplete data were not reported here. Tumor staging in this study did not incorporate depth of invasion, as specified in AJCC 8th edition guidelines, as this information was not available in retrospectively reviewed pathology reports at our institution prior to 2018 [33]. Tumor depth is another important dimension that could significantly alter the overall ablative defect that should be considered in similar future QOL studies [34–36]. Notably, no patient in our cohort was edentulous. As such, the dental status of the patient does not appear to be likely confounding these results.

Conclusion

In this limited sample QOL study, we establish postsurgical PROMs for T1–2 FOM tumor defects reconstructed with STSG. Overall, patients with STSG reconstruction reported acceptable outcomes in swallowing and speech with few functional outliers, thus reinforcing this reconstructive method as a reasonable option for these early FOM tumors. Worse chewing was reported by A-FOM patients relative to L-FOM and MM-FOM, suggesting that this subsite may be less suitable for STSG reconstruction. A different type of reconstruction may result in better functional outcomes for A-FOM. Larger multicenter studies are necessary to delineate more clearly the role of STSG relative to other reconstructive methods in the head and neck surgeon's reconstructive algorithm.

Statement of Ethics

This study protocol was approved by the Institutional Review Board of the UCSF Medical Center (IRB #17-22646). All subjects have given written informed consent for participation in this research study. This research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

Patrick Ha, MD, is on the advisory board for Bayer/Loxo Oncology. He has received grant funding from Stryker, Synthes, and Medtronic. WillIam Ryan, MD, is on the scientific advisory boards for Medtronic, Olympus, and Rakuten. All other authors have no declarations of interest.

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Author Contributions

Andrew Larson: project conception, data analysis, primary manuscript drafting and revision, and manuscript final approval; Mary Han: data collection, analysis, patient recruitment, database management, and manuscript final approval; Katherine Webb: patient recruitment, data collection, database management, and manuscript final approval; Edgar Ochoa: patient recruitment, data collection, database management, and manuscript final approval; Gaelen Stanford-Moore: project design and conception, manuscript editing, critical revisions, and final approval; Ivan El-Sayed: critical manuscript editing, intellectual contributions to project design, and manuscript final approval; Jonathan George: critical manuscript editing, intellectual contributions to project design, and manuscript final approval; Patrick Ha: critical manuscript editing, intellectual contributions to project design, and manuscript final approval; Chase Heaton: critical manuscript editing, intellectual contributions to project design, and manuscript final approval; William Ryan: project conception and oversight, manuscript drafting, editing, and final approval.

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