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

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Abstract

Objectives To establish 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. Design Retrospective analysis with a validated questionnaire Setting Tertiary academic cancer center Participants Patients with pathologic stage T1/T2 FOM-CA who underwent resection and STSG reconstruction Main Outcome Measures University of Washington QOL (v4) questionnaire completed after at least 6 months since surgery Results 24 out of 49 eligible patients completed questionnaires with a mean follow up of 41 months (range: 6-88). Subsites of tumor involvement/resection included: 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 or better ("I cannot swallow certain solid foods"). 96% (23/24) reported speech of 70 or better ("difficulty saying some words, but I can be understood over the phone"). A-FOM patients reported worse chewing than L-FOM patients (mean: 50.0 vs. 85.3; p = 0.01). All four 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. Conclusions STSG reconstructions for pathologic T1-T2 FOM-CA appear to result in reasonably high PROM QOL outcomes with the exception of A-FOM tumors having worse chewing outcomes.

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Retrospective analysis with a validated questionnaire

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24 out of 49 eligible patients completed questionnaires with a mean follow up of 41 months (range: 6-88). Subsites of tumor involvement/resection included: 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 or better ("I cannot swallow certain solid foods"). 96% (23/24) reported speech of 70 or better ("difficulty saying some words, but I can be understood over the phone"). A-FOM patients reported worse chewing than L-FOM patients (mean: 50.0 vs. 85.3; $p = 0.01$). All four 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.

Conclusions

STSG reconstructions for pathologic T1-T2 FOM-CAappear to result in reasonably highPROM QOL outcomes with the exception of A-FOM tumors having worse chewing outcomes.

Key Points

- 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 previously established.
- We have performed a retrospective analysis of responses in relevant symptomdomains of the University of Washington Quality of Life (v4) questionnaire from patients having undergone resection and STSG reconstruction of pathologic stage T1/T2 FOM-CA.
- In general, STSG reconstructions for pathologic T1-T2 FOM-CAappear to result in reasonably high-PROM QOL outcomes in swallowing and speech at least 6 months past surgery.
- Chewing outcomes were uniformly worse among the patients with defects of the anterior floor of mouth relative to the other oral cavity subsites studied, which included the lateral FOM and alveolar ridge with FOM.

Keywords

Head and neck cancer; quality of life; skin grafting; oral cavity; reconstructive surgery; floor of mouth; squamous cell carcinoma

INTRODUCTION

For ablation defects of early stagefloor of mouth carcinoma(FOM-CA),reconstructive options includesecondary intention, split thickness skin graft (STSG), local/regional pedicled flaps, and microvascular free flaps (FF), 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, STSGsare likely being used less and less forreconstruction. The outcomes of STSGs for FOM-CA defects are not well studied. Past studiesof 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 outcomes studies. Detailed PROMs ofSTSG 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 factorsrelated to FOM STSG reconstruction QOL outcomes are also unclear. Given thesegaps, we conducted a study of patient reportedQOL outcomes after STSG reconstruction ofearly clinical T-stage (cT1/T2) FOM-CAdefects.

MATERIALS AND METHODS

Patient Recruitment

We recruited all living patients, at least 18 years old,with a history of pathologic T1-2 FOM-CA who had undergoneFOM resection with possible partial glossectomy and/or marginal mandibulectomy (MM) and reconstruction with a thigh STSGat the [REMOVED FOR BLIND PEER REVIEW]Medical Center from August 2011 to October 2018 with at least 6 months 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.

Outcome Measures

Patients were asked to complete the University of Washington Quality of Life Questionnaire Version 4 (UW-QOL) 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 0-100 with a high score representing a high/healthy level of functioning. Demographic and clinicopathologic characteristics, and clinical outcomes were extracted from a retrospective chart review.We 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]

Surgical Methodology

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 bolsterwas sutured over the STSGin the FOM and then removed at 5-7 days postoperatively (Figure 1).The donor site from the STSG from the inguinal regionis excised in an elliptical fashion and closed primarily for a cosmetically favorable linear incisionin the inguinal crease (Figure 2).

Statistical Methods

QOL responses were compared with a two-tailed student's t test between domains of interest using a pre-defined 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 the cohort of patients who underwentreconstruction by various methods.[17,18]Statistical analyses were performed using RStudio Version 1.1.442.

RESULTS

24out of 49(49%) recruited alive patients completed questionnaires. There were 3 patient subsetsbased 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 underwenta lateral marginal mandibulectomy (MM-FOM)(n = 3). There were no A-FOM or L-FOMpatients who also underwent a marginal mandibulectomy. The anatomic categories were determined upon surgeon description of subsite involvement/resection in the original operative report, with the mandibular canine defining the border between the anterior and lateral FOM.

Table 1describespatient, tumor, and treatment factors of the cohort. There were no significant difference between average follow up times of L-FOM and A-FOM (39.2 vs. 32.5 mos.; 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 mos., p=0.24). None of the patients in the cohort were edentulous. There were no complete STSG graft losses reported.

Table 2 shows the comparisonof our study patient cohort, the normative patient cohort, and the Kazi*et al.* cohort. In comparison with the normative patient cohort, our patient cohort reported significantly worse outcomes in appearance, swallowing, chewing, speech, taste, and saliva. Relative to the outcomes data

on partial glossectomy patients by*Kazi et al.* (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;$p = 0.01$). All4of the A-FOM patients each reported a chewing score of 50that 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.

The8 (33%) patients in the study cohortwho underwent adjuvant XRTreported significantly worse appearance(mean 62.5 vs. 89.0, respectively; p <0.01).Otherwise, there was no significant differencebetween reported outcomes in swallowing, chewing, speech, and all other reported symptom domains (Table 3). There was no difference in average follow up times between non-irradiated and radiated patients: mean 37.3 months versus 48.9 months, respectively($p = 0.31$).

Patients with early follow up (6-12 mos.; n = 4) vs. late follow up (12+ mos.; n = 20) were compared. There was no difference in reported swallowing between early vs. late follow up, respectively for swallowing (mean 100.0 vs. 85.0, $p = 0.07$)withall early follow up patients reporting the highest score in swallowing (100),chewing (mean87.5 vs. 77.5, $p = 0.48$), speech (mean70.0 vs. 72.5, $p = 0.74$), taste (mean85.0 vs. 67.0, $p = 0.23$), or saliva (mean85.0 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.*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, thenon-irradiated 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 chewing (mean 83.3 vs. 94.0,$p = 0.07$), respectively. In comparison to the Kazi*et al.* post-glossectomy patients, there wereno 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 didevaluate the lowest-scoring patients in each category. There was only one 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. 42% (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 of50), while 4 of the patients scoring 50 (40%) had undergone adjuvant radiation. None of the patients in our cohort reported swallowing less than 70 ("I cannot swallow certain solid foods"). 42% (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").

DISCUSSION

Novelty of Study

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 canpotentiallylower 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.

Synopsis of Key Findings and Comparisons with Other Studies

Overall, irrespective of FOM subsite and adjuvant radiation,most patients in this study reported acceptable results in swallowing and speech. A majority of patients reportedtotally normal swallowing with all patients reporting at least near normal swallowing. There was only one negative outlier in the speech symptom category (an A-FOM patient without adjuvant radiation).The STSG reconstruction patients,compared to the normative population sample, did report worse performance in chewing, swallowing, speech, and saliva;thus, this reconstruction method does not generally achieve baseline functions according to the patients. 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 mandibulectomywithout 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.* 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.* were not reported according to reconstructive method. However, this comparison contextualizes the outcomes of our STSG patients. We infer from our data and the comparisonthat STSG for T1-T2 FOM carcinomaappears to be a reasonable reconstructive option from a QOL perspective with outcomes on par if not better than a more general cohort of partial glossectomypatients.

Our data suggests that A-FOM may be less appropriate for STSG reconstruction than other subsites, given that chewing was reported to be worse that 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 or free flap 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 non-irradiated patients would be a subset whose oral cavity functionwould 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,anddid 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.

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 donorsite 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.

Study Limitations

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, free flap 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 FF 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 allow 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, this incomplete data was 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 alters the overall ablative defect that should be considered in similar future QoL studies. [34-36]Notably, no patient in our cohort wasedentulous. 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 PROMsfor T1-2FOM tumor defects reconstructed with STSG. Overall, patients with STSG reconstruction reported acceptable outcomes in swallowing and speech with few functional outliers. Worse chewing was reported by A-FOM patients suggesting that a different type of reconstruction may possibly result in better outcomes. Larger multicenter studies are necessary todelineate more clearly the role of STSG relative to other reconstructive methods in the head and neck surgeon's reconstructive algorithm.

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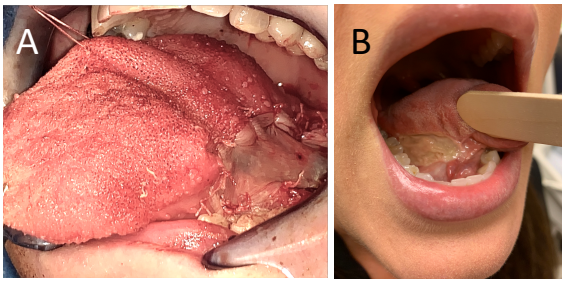
FIGURE LEGENDS

Figure 1:STSG reconstruction of lateral tongue and FOM . Representative photo intraoperatively following STSG inset (A) and postoperatively with characteristic well-healed appearance (B). Note: photos are not taken from the same patient.

Figure 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).

Figure 3: QoL Outcomes according to subsite. Three oral cavity subsites reconstructed with STSG including L-FOM, A-FOM, and MM-FOM are compared by QoL symptom categories, relative to normative population data. Error bars indicate 95% confidence interval.



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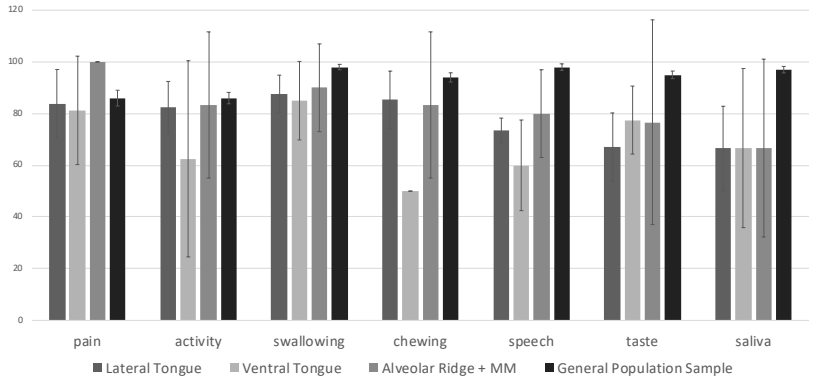

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