Background: Submental artery island flap (SMIF) has gained acceptance as a simple and reliable option in oral reconstruction. However, there are unsettled concerns regarding its safety in oral cancer because of insufficient data in the literature.

Aims: To analyse the oncological safety of SMIF in oral reconstruction and to study the patterns of locoregional failure and overall survival.

Materials and methods: Prospectively collected data of 229 patients with oral cancer who underwent reconstruction using SMIF from October 2004 to September 2012 in a large volume, low resource centre was analysed for locoregional recurrence and long term survival.

Results: Study population included 122 males and 107 females, with mean age of 56.12 years. The primary site was tongue in 79.47%, floor of mouth in 11.35%, buccal mucosa in 5.2%, alveolus in 3.49% and lip in 0.4% of the patients. Majority of patients (78.16%) presented with tumour staged T2 or less. Seventy-four (32.3%) patients had clinically palpable neck nodes preoperatively, of which twenty eight had involvement of level Ib. Marginal mandibulectomy was combined in fifty one (22.3%) cases available. Sixteen cases had flap loss of which, 4 were total. Eleven male patients had persistent hair growth on the flap. There were no donor site morbidity.

Selective or Modified Radical Neck dissections were performed in 94.4% of the patients, whereas the remaining 5.6% had only level I clearance. Seven (3.1 %) patients required bilateral neck dissection. After pathological examination fifty two (22.7%) patients had proven nodal metastasis. Most of the clinically positive nodes (fifty six out of seventy four) were negative in the final histopathology report.

After a median follow up of 51.6 months (ranging from 5.5 to 107.5 months), thirty nine patients had locoregional recurrence - twenty one (9.2%) with primary site involvement and eighteen (7.8%) in the neck alone. Among patients who had nodal recurrence, nine failed in level 1b. Two of them had recurrence at primary site as well - one at the flap site and one away from it. Six of the eighteen nodal recurrences occurred outside the field addressed earlier. Seven (3.1%) patients had distant metastasis. Of the total locoregional recurrences ten patients could be salvaged surgically.

On univariate analysis of variables for locoregional recurrence, statistical significance was found for clinical node involvement (p value = 0.017), tumour differentiation (p value= 0.01), pathological node positivity(p value=0.003) and pathological T staging(p value =0.05). Multivariate analysis showed significance for tumour differentiation (p value = 0.05) and pathological node positivity(p value = 0.002).
The overall survival of this series of patients was found to be 97.8 +/- 1.0 % at 1 year, 89.6% +/- 2.1% at 3 years and 84.6 +/- 2.7% at 5 years and disease free survival was 88.6 +/- 2.1 % at 1 year, 81.8% +/- 2.6% at 3 years and 78.1 +/- 3.0% at 5 years. This rate is comparable with the available data on survival.

**Conclusion:**

Submental artery island flap harvested after meticulous dissection of the pedicle is oncologically safe in carefully selected oral cancers.
FUNCTIONAL AND QUALITY OF LIFE OUTCOMES AFTER GLOSSECTOMY: A MULTI-INSTITUTIONAL STUDY OF THE HEAD AND NECK RESEARCH NETWORK

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Background: Communicative, swallowing and social outcomes are important indicators of the overall outcomes after surgical resection and reconstruction of the oral cavity. The question of how patients recover their communicative function, swallowing outcomes, and quality of life after primary surgery for tongue cancer over the course of the first year of survivorship was one of the first target research areas for the Head and Neck Research Network (HNRN). The HNRN is comprised of a diverse group of professionals who are interested in the areas of functional outcomes, quality of life, and economic costs as they relate to survivorship after treatment for head and neck cancer.

Objective: to report on the patient reported functional and quality of life outcomes of partial glossectomy patients enrolled in the HNRN-02 protocol.

Methods: The study was conducted at the three HNRN centers, located in Canada, United States, and Finland. All centers obtained the appropriate institutional ethics approval from their respective centers. All patients undergoing primary surgery for oral cavity squamous cell carcinoma were recruited into the study. Only patients whose final surgical defect comprised a partial glossectomy with or without resection of the floor of mouth were included in the study. Patients whose defects involved the mandible, other oral cavity subsites, a total glossectomy, or the oropharynx were excluded. Patient-reported data was collected. Three tools were used to collect outcomes: the Speech Handicap Index was used to assess patient perception of communicative function; the MD Anderson Dysphagia Inventory was used to assess swallowing outcomes, and the EORTC Quality of Life Questionnaire Head and Neck Module (EORTC QLQ-H&N35) was used to measure quality of life. Assessments took place at 3 different time points: pre-treatment, and 6- and 12-months post-operative.

Results: 98 patients from across all three centers completed the 3-year study. All patients had free tissue transfer reconstruction. Preliminary results suggest that while patient-reported speech and swallowing outcomes do not differ from the pre-treatment to the final assessment time, quality of life outcomes do. The decrease of quality of life seems to be related to the adjunct postoperative treatment.

Conclusion: HNRN-02 demonstrates the feasibility of performing prospective head and neck cancer and reconstruction trials as an international network. Patients undergoing partial glossectomy with reconstruction report a return to their pre-treatment function at 1 year. Patients have a decrease in quality of life related to adjunctive treatment.
INDIVIDUALIZED RISK ESTIMATION OF POSTOPERATIVE COMPLICATIONS FOLLOWING SURGERY FOR ORAL CAVITY SQUAMOUS CELL CARCINOMA

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Introduction: Postoperative complications following ablative head and neck surgery carry the potential for serious morbidity, and are challenging to anticipate in the preoperative setting. The aim of this study is to develop a statistical tool capable of predicting an individual patient’s risk of developing a major complication following ablative surgery for oral cavity squamous cell carcinoma (OCSCC).

 Patients: Previously-untreated adult patients with biopsy-proven OCSCC who underwent ablative surgery from 2007 to 2012 at a comprehensive cancer center (n=506).

Methods: This retrospective case series is derived from an institutional clinical oncologic database augmented by chart abstraction. The primary endpoint was a major postoperative complication requiring invasive intervention (grades III-V) as defined by the Clavien-Dindo classification. The postoperative period was defined as the time interval from the date of surgery to either the date of discharge from the hospital or forty-five days after surgery, whichever occurred later. Patients treated between 2009 and 2012 (n=354; 70%) comprised the modeling cohort and were used to develop a nomogram to predict the risk of developing the primary endpoint. Thirty-five patient, tumor, and treatment variables were abstracted from the medical records. Univariate analysis and correlation analysis were used to prescreen the predictors for incorporating in the subsequent multivariable logistic regression analysis. Mice method was employed to impute missing values before conducting multivariable analysis. The variables with the highest predictive value were identified with Stepdown model reduction method and included in the nomogram. Patients treated in 2007 and 2008 (n=152; 30%) were used to validate the nomogram. Concordance index was calculated to measure discrimination ability, with bootstrapping to correct for overfitting bias.

Results: Thirty-six (10%) patients in the modeling cohort and 16 (11%) patients in the validation cohort developed a major postoperative complication. Clinical characteristics remained similar between the two cohorts (p > 0.05 for all comparisons). Six preoperative variables with the highest individual predictive value (body mass index, Washington University Head and Neck Comorbidity Index [WUHNCI], white blood cell count, hematocrit, planned neck dissection, and planned tracheostomy) were incorporated within the nomogram. The nomogram predicted a major complication with a validated concordance index of 0.79. Inclusion of surgical operative variables, such as time under anesthesia, in the nomogram maintained its predictive value, with a concordance index of 0.77 (p = 0.616).

Conclusions: We have developed a powerful statistical tool that is highly accurate in estimating an individual patient's risk of developing a major complication following surgery for OCSCC.
BACKGROUND:

An association between the survival of patients with oral cavity squamous cell carcinoma (OCSCC) and advancements in diagnosis and therapy has not been established.

METHODS:

This was a retrospective, longitudinal, international, population-based study of 2738 patients who underwent resection of OCSCC during 2 different decades. Characteristics of patients from 7 international cancer centers who received treatment between 1990 and 2000 (group A; n = 735) were compared with patients who received treatment between 2001 and 2011 (group B; n = 2003).

RESULTS:

Patients in group B had more advanced tumors and tended to develop distant metastases more frequently than patients in group A (P = .005). More group B patients underwent selective neck dissection and received adjuvant radiotherapy (P < .001). Outcome analysis revealed a significant improvement in 5-year overall survival, from 59% for group A to 70% for group B (P < .001). There was also a significant improvement in disease-specific survival associated with operations performed before and after 2000 (from 69% to 81%, respectively; P < .001). Surgery after 2000, negative margins, adjuvant treatment, and early stage disease were independent predictors of a better outcome in multivariate analysis. The decade of treatment was an independent prognostic factor for cancer-specific mortality (hazard ratio, 0.42; 95% confidence interval, 0.3-0.6).

CONCLUSIONS:

The survival rate of patients with OCSCC improved significantly during the past 2 decades despite older age, more advanced disease stage, and a higher rate of distant metastases. The current results suggest that the prognosis for patients with OCSCC has improved over time, presumably because of advances in imaging and therapy. Cancer 2013. © 2013 American Cancer Society.
SURVIVAL EVALUATION IN ADVANCED STAGE (STAGE III-STAGE IV) ORAL SQUAMOUS CELL CARCINOMA PATIENTS TREATED WITH MULTIMODAL THERAPY- AN EXPERIENCE IN ASIAN INDIAN POPULATION.

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Advanced stage oral squamous cell carcinoma (OSCC) remains a challenging disease to treat. Primary ablative surgery followed by post-op radiotherapy (S-RT) remains the mainstay of treatment at various centers. Despite this aggressive dual modality therapy, the disease outcomes have remained constant at 30% local or regional disease recurrence, 25% distal metastasis and 30% 5 year survival.

A retrospective analysis of survival rates of patients having advanced stage OSCC treated with multimodal therapies (Primary tumor ablation and neck dissection followed by post-op radiotherapy (S-RT) or combined chemo-radiation (S-CRT) was performed to analyze the outcome of these modalities for patient survival and whether addition of postoperative chemotherapy (S-CRT) improves survival as compared to other treatment regimens. The major indicators of prognosis were analysed such as location of the primary tumor, TNM staging, stage at initial presentation, therapeutic approach, type of neck dissection, and tumor recurrence.

Demographic, pathologic, treatment modality and survival data of 124 patients (from June 2008 - June 2013) treated at our institute was included in the study for analysis. Patients were grouped by treatment modality. All primary tumor ablations were followed by neck dissections. 69 patients received S-RT while 55 patients were opted for S-CRT. Overall survival, disease specific survival, disease free survival was estimated with Kaplan- Meier analysis and compared between groups (S-RT and S-CRT) with Cox regression analysis.

Survival was significantly influenced with the type of modality, location of primary tumor and regional spread of disease. Patients receiving S-CRT had improved overall, disease specific, disease free and metastasis free survival as compared to S-RT group (p<0.05). A survival advantage of 11% was achieved in S-CRT group as compared to S-RT group even in patients with extra-capsular spread (ECS) and perinural invasion (PNI). Hence, addition of adjuvant chemotherapy to S-RT improves survival outcomes in advanced OSCC, especially in patients with regional spread of disease.
SURGICAL SALVAGE FOR RECURRENT ORAL CAVITY SQUAMOUS CELL CARCINOMA

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Importance: In patients with oral cavity squamous cell carcinoma (OCSCC), the impact of a recurrence on survival is profound, with median survival 12-16 months. Multidisciplinary teams must carefully weigh harm versus benefit when considering options for recurrent OCSCC given potentially high morbidity and cost of treatment.

Objective: Identify patient, tumor, and treatment related characteristics associated with decreased survival in patients with recurrent OCSCC.

Design: Retrospective Chart Review

Patients: 401 patients with locally recurrent (with or without regionally recurrent) oral cavity squamous cell carcinoma without distant metastases

Setting: Tertiary care cancer center

Main Outcome Measures: Primary outcomes evaluated were overall and recurrence-free survival. Variables assessed included original and recurrent T and N stage, original and recurrent treatment, disease free interval, and local, regional, and distant second recurrences. Speech and swallowing outcomes evaluated in the surgical cohort included decannulation rate, percent speech intelligibility, and percent of patients with gastrostomy tube and an oral diet. Professional and hospital charges associated with salvage surgery were reviewed.

Results: 2104 patients with OCSCC presented to MD Anderson Cancer Center from 1996-2010, of which 808 had recurrent or residual disease. 401 patients had locally recurrent (with or without regionally recurrent) disease without distant metastases, with a mean follow up of 29 months (standard deviation 37 months) after diagnosis of recurrent disease, and 30% alive at 5 years after recurrence. Factors associated with decreased survival included a disease free interval of < 3 months (p=0.0006), advanced recurrent T (p=0.0014) and N stage (p<0.0001), extension of recurrent primary tumor to the tongue base (p=0.0129), and history of radiation therapy in the initial treatment of disease (p=0.0012). Of the patients with locally recurrent disease without distant metastases, 250 underwent surgical salvage while 151 were treated nonsurgically with palliative intent. 5-year overall survival among surgical salvage patients was 44%. For patients undergoing surgical salvage, 126 (50%) developed a second recurrence a mean of 17 months after surgical salvage. Thirty-eight (15%) required an additional surgery for a complication within 3 months of initial surgical salvage. 148 patients had perioperative tracheostomy tubes placed and 78% (n=116) were decannulated. Postoperative speech and swallowing assessments revealed 95% (n=238) of patients had >50% speech intelligibility and 81% (n=204) tolerated some oral intake, with 71% (n=178) having an oral diet without gastrostomy tube. The mean and median charges for patients who underwent surgical salvage were $99,955 (standard deviation $78,199) and $90,463 (range $6,451-$668,058) respectively.
Conclusions: Locally recurrent OCSCC is associated with poor overall survival and high cost of treatment, but selected patients are good candidates for surgical salvage with acceptable functional outcomes. Several clinicopathologic factors predict poor outcomes including advanced recurrent T and N stage, short disease free interval, extension of the recurrent primary tumor to the tongue base, and previous radiation therapy. Patients with small volume recurrences not involving the tongue base with minimal neck disease, that occur greater than 3 months after completion of treatment and without history of radiation therapy, appear to be the optimal candidates for salvage surgery.
OUTCOMES OF SALVAGE OF LOCOREGIONAL RECURRENT AFTER SURGICAL RESECTION OF ORAL CAVITY SQUAMOUS CELL CARCINOMA

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Background: Successful salvage of recurrent disease remains a challenge in the management of oral cavity squamous cell carcinoma (OCSCC), despite advancements in treatment. The aim of this study is to describe the fate of patients who are successfully salvaged following their first local and/or regional recurrence.

Patients: All patients who underwent curative surgery without adjuvant therapy for OCSCC between 1985 and 2012 at a comprehensive cancer center and subsequently developed local and/or regional recurrence without distant metastasis (n=309).

Methods: Clinical, pathologic, and outcomes data were abstracted from a pre-existing computerized database and verified with chart review. Twenty-two patients were excluded due to the development of a second head and neck primary or inadequate information. Of the 287 patients remaining for analysis, 39 (14%) were not salvageable. Disease free interval (DFI) was defined as time from primary operation to first locoregional recurrence (fLRR). Details of salvage treatment were recorded for each patient and then subsequent cancer specific mortality (sCSM) and subsequent recurrence free survival (sRFS) were determined using the Kaplan Meier method. Factors predictive of sCSM and sRFS were identified by multivariate analysis.

Results: Median DFI prior to fLRR was 9.3 months (range 0.8-302.5). Median follow-up after fLRR was 20.7 months (range 0.1-337.3). The site of first recurrence was the primary site in 149 (52%) patients, regional nodes in 112 (39%), and both in 26 (9%). Patients who were not salvageable were more likely to be older than 60 years of age (p=0.05), have a DFI <9.3 months (p=0.007), have advanced initial T classification (p=0.001), and have nodal metastasis at initial surgery (p=0.001) than patients who were salvageable. Non-salvageable patients were also more likely to fail locoregionally than either locally or regionally (p=0.001). The 1 year CSM for non-salvageable patients was 7.9%, while the 2 year CSM after salvage was 68.8% (p<0.001).

Of 248 patients amenable to salvage, 116 (47%) had surgery alone, 105 (42%) had surgery and adjuvant therapy and 27 (11%) had radiation +/-chemotherapy. The 2-year sRFS and sCSM were 55.4% and 66.7%, respectively. Forty-seven percent of these patients recurred again, with a median time to recurrence of 7.0 months (range 1.5-108.3). Initial T4 classification (p<=0.016), initial nodal metastasis (p<=0.001), DFI shorter than 9.3 months (p<=0.024), and treatment of fLRR including non-surgical modalities (p<=0.008) were univariate predictors of sRFS and sCSM. Synchronous locoregional recurrence was a univariate predictor of sCSM (p=0.005) as well. On multivariate analysis, T4 classification (HR 3.000, p=0.002) and synchronous locoregional recurrence (HR 2.704, p=0.010) were predictive of worse sCSM. There were no significant predictors of sRFS on multivariate analysis.

Conclusion: Recurrences after successful salvage of local and/or regional recurrences are not uncommon in patients with OCSCC. Patients with initially advanced tumors and those who fail concurrently at the primary site and at the neck have the bleakest outcomes.
Neck metastasis is associated with the prognosis and survival in oral cancer. Almost neck lymphatic drainage was from level I to 5.

Objective: This paper aims to evaluate the correlation between each levels and lymph node metastasis in patients with oral carcinoma. And the relation between total count of lymph node and metastasis was also be evaluated.

Method: There were 1450 observations finished operation involved all five levels. 218 subjects accepted single side, left or right, and 71 subjects accepted two side. 275 subjects were males with average age of 52.15±9.86 years and 15 were females with average age of 58.29±11.51 years. Of total subjects, 112 (38.62%) were buccal cancer, 72 (24.83%) were tongue cancer, 63 (21.72%) were gingival, 16 (5.52%) were palate and last 27 (9.31%) were classified into others. The correlation between level and lymph node metastasis or total count of lymph node and lymph node metastasis was performed by generalized estimating equation, assuming poisson distribution and unstructured correlation structure. Magnitude of strength of association was reported by odds ratio. All statistic assessments were evaluated at the 0.05 level of significance. Statistic analyses were performed using SAS 9.2 statistics software.

Results: After adjustment of tumor site, level was significant correlated with lymph node metastasis. The risk of lymph node metastasis in level 1 was 23.37 time than level 5 (P<0.001). The risk of lymph node metastasis in level 2 was 14.62 time than level 5 (P<0.001). And the risk of lymph node metastasis in level 3 was 6.13 time than level 5 (P=0.011). No significant difference between level 4 and level 5 in lymph node metastasis. The average total count of lymph node was 8.98±5.10 (range from 1 to 25) in metastasis group and 8.16±5.40 (range from 1 to 72) in non-metastasis group. After tumor site and level were adjusted, no significant correlated was found in total count of lymph node and lymph node metastasis.

Conclusion: There is significant difference on neck metastasis between neck level I,II,III compared with level V in oral cavity cancers. And average metastasis rate was decreasing from level I to level 5. There was no relationship between total count of lymph node and lymph node metastasis.
OUTCOMES OF PATIENTS TREATED WITH MULTIMODAL THERAPY FOR RECURRENT ORAL CAVITY CANCER
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Introduction:
Primary management for early stage squamous cell carcinoma of the oral cavity is typically surgery alone; adjuvant radiation is recommended infrequently due to high rates of local-regional control. However, recurrences can occur. This study was designed to evaluate the outcomes of patients with recurrence following surgery who are managed with multimodal therapy.

Methods:
The database of patients irradiated at The University of Texas MD Anderson Cancer Center was searched for patients with oral cavity cancer who developed a local-regional recurrence after primary surgery alone between 2000 - 2012. Statistical methodology included frequency tabulation and Kaplan-Meier testing to determine survival rates.

Results:
The cohort consisted of 84 patients who developed local-regional recurrence after primary surgery. Forty-three patients had a history of premalignant lesion prior to developing an invasive cancer. Stage of patients at initial surgery included 60 patients with T1; 16 patients with Tx; 8 patients with T2. Only 3 patients were node positive (N1). Primary site distribution was as follows: oral tongue 55 patients (66%), floor of mouth 9 (11%), gingiva 7 (8%), buccal 5 (6%), retromolar trigone 4 (5%) and lip 4 (5%). The median time from initial diagnosis to recurrence was 1 year. Seventeen patients had primary site recurrence; 41 patients neck recurrence; and 26 patients both primary and neck recurrence. Among the 66 patients with neck recurrence, 18 had recurrence in an operated neck and 22 had recurrence in the contralateral neck (including 10 patients with rN2c). 78 patients had surgery for their recurrent disease followed by radiation therapy and 6 were treated with chemotherapy and radiation. Among the 84 patients who received radiotherapy, 66 were treated to the primary site and neck, and 18 to the neck alone. The median radiation doses to the primary and neck were 60 Gy and 60 Gy, respectively. Fifteen patients received induction chemotherapy; 56 patients received concurrent chemotherapy.

The median follow-up time was 34 months (range 3 - 127 months). The 2-year actuarial overall survival, local-regional control and progression-free survival rates were 70%, 65% and 52%, respectively. When analyzed by site or recurrence (primary only, neck only or both primary and neck) there were no statistical differences in outcomes. There was no survival advantage to patients who received chemotherapy.

Conclusion:
In this cohort of early stage oral cavity squamous cell carcinoma patients treated with surgery and presenting with recurrent disease requiring multimodal therapy, half presented with metachronous isolated nodal disease, and half had a history of premalignancy. Further therapy in radiation-naïve
patients with recurrent oral cavity cancer is feasible. Disease control and survival rates are modest after multi-modal therapy including radiation, and are relatively similar to rates expected for patients who present de novo.