



The effect of reconstruction on positive margin rates in oral cancer: Using length of stay as a proxy measure for flap reconstruction in a national database

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Abstract

Importance:
Locoregional recurrence remains an important site of treatment failure in oral cavity squamous cell carcinoma (OCSCC) and has been associated with positive margin resections. The availability of pedicled or free flap reconstruction may provide the ablative surgeon with the flexibility to take larger surgical margins. The effect of planned flap reconstruction on positive margin rates in OCSCC has not been well studied.

Objective:
To determine if length of stay (LOS), as a proxy measure for flap reconstruction, is associated with positive margin rates in OCSCC surgery.

Design and Setting:
Retrospective review of the National Cancer Database (NCDB), 2004-2015

Participants and Exposures:
Included patients undergoing surgery for previously untreated clinical T1-3 OCSCC. Post-operative LOS was dichotomized between ≤4 and >4 days as a proxy measure for whether patients may have received flap reconstruction. Although patients with a LOS of >4 days represent a diverse group, they are overall more likely to have undergone flap surgery than those with a LOS ≤4 who are very unlikely to have had an oral cavity flap reconstruction.

Main Outcomes and Measures:
Factors associated with positive margin rates and overall survival.

Results:
10,107 patients were included who underwent primary surgery for OCSCC, of which 5,290 (52%) were clinical T1 and 4,852 (48%) were clinical T2-3. LOS was ≤4 for 6915 (68%) patients and >4 days for 3192 (32%) patients. 771 (8%) patients had a positive surgical margin. In a multivariable logistic regression analysis, LOS ≤4 days was significantly associated with a positive margin resection in patients with clinical T2-3 tumors (OR 1.68, 95%CI 1.37-2.06) compared to patients with LOS >4 days. However, LOS was not associated with surgical margin status in patients with clinical T1 disease (OR 0.76, 95%CI 0.55-1.06). In a multivariable survival analysis, regardless of clinical stage, patients with positive margin resections demonstrated worse overall survival (cT1: HR 1.35, 95%CI 1.06-1.72; cT2-3: HR 1.52, 95%CI 1.33-1.74).

Conclusion:
LOS >4 days after oral cavity cancer resection was significantly associated with negative surgical margins in clinical T2-3 oral cavity cancer. This suggests the possibility that patients undergoing flap reconstruction after resection have fewer positive surgical margins.

Introduction

- Oral cavity and lip cancers accounted for 2% of new cancer diagnoses and worldwide cancer deaths in 2018 [1]
- In the US, there were more than 35,000 new oral cavity cancers in 2019, with nearly 7500 deaths [2]
- 5- year survival from 2008 to 2014 was only 65% [2]
- Positive surgical margins increase locoregional recurrence and decrease survival [3]
- While surgical margin status is influenced by tumor aggressiveness and growth patterns [4], surgical technique have at least some role in margin status
- Studies examining this have been single-institution retrospective examinations with cohorts plagued by confounding [5]

Hypothesis

- Planned pedicled or free flap reconstruction allows the ablative surgeon to take more aggressive margins, decreasing positive margins

Materials & Methods

- Patient selection**
- 2015 NCDB analyzed for patients diagnosed with T1-3 OCSCC between 2004 and 2015; 10,107 patients analyzed
 - Excluded: prior malignancy, M1, gross residual tumor, non-traditional adjuvant therapy, missing data, LOS >14 days
- Cohort definition**
- NCDB does not include reconstruction data, so hospital LOS dichotomized to ≤4 days or >4 days as proxy measure
 - LOS ≤4 days: highly unlikely to have vascularized reconstruction
 - LOS >4 days: diverse group including patients with co-morbidities, advanced age, but majority of patients with flap reconstruction should be in this group
 - Dichotomized to T1 and T2-3 – margin status on T1 tumors less likely to be affected by reconstruction
- Data Analysis**
- SPSS for multivariable logistic regression and survival analysis

Results

Table 1: Multivariate Analysis

Factor	Positive Margin HR (95% CI)		Survival HR (95% CI)	
	cT1	cT2-3	cT1	cT2-3
Age (<61 vs ≥61)			0.67 (0.57-0.77)*	0.72 (0.65-0.80)*
Insurance (private vs other)	0.79 (0.61-1.03)	0.76 (0.63-0.93)*	0.58 (0.49-0.67)*	0.64 (0.57-0.71)*
Facility type (Academic cancer center vs other)		0.61 (0.50-0.74)*	0.77 (0.68-0.88)*	0.84 (0.76-0.93)*
Charlson-Deyo comorbidity index (0 vs ≥1)			0.80 (0.70-0.93)*	0.73 (0.66-0.81)*
Clinical T-stage (cT2 vs cT3)	n/a	0.69 (0.55-0.86)*	n/a	
Pathological T-stage (pT1 vs pT2 or greater)	0.56 (0.40-0.80)*	0.51 (0.39-0.69)*	0.70 (0.58-0.85)*	0.56 (0.49-0.65)*
Pathological N-stage (pN0/x vs pN+)	0.81 (0.58-1.13)	0.69 (0.56-0.83)*	0.55 (0.45-0.66)*	0.44 (0.40-0.50)*
Length of stay (≤4 days vs >4 days)		1.68 (1.37-2.06)*	0.79 (0.67-0.93)*	0.96 (0.87-1.06)
Depth of invasion (<4mm vs ≥4mm)	0.80 (0.62-1.03)	0.78 (0.64-0.95)*	0.86 (0.76-0.98)*	
Margin status (positive vs negative)	n/a	n/a	1.35 (1.06-1.72)*	1.52 (1.33-1.74)*
Subsite (oral tongue vs other)	0.48 (0.37-0.62)*	0.48 (0.39-0.58)*		
Tumor grade (low vs high)	0.67 (0.50-0.90)*	0.66 (0.50-0.87)*	0.70 (0.60-0.82)*	0.71 (0.62-0.82)*
Adjuvant radiation	n/a	n/a	1.24 (1.03-1.50)*	0.87 (0.77-0.98)*
Adjuvant chemotherapy	n/a	n/a	1.28 (0.99-1.64)	1.07 (0.94-1.22)

No value: no significant difference on univariate analysis, not included in multivariate analysis; *: significant difference on multivariate analysis

Discussion

- Large sample size allowed analysis of cT1 tumors separate from cT2-3 tumors
- Vascularized reconstruction should not impact ability to clear margins for cT1 tumors, but may for cT2-3 tumors
- Factors besides flap reconstruction that increase hospital LOS (co-morbidities, age, complications) would decrease survival and could *increase* positive margins
 - Low volume surgeon (increased positive margins) at hospital without resources for prompt discharge (longer LOS)
 - Surgeon foregoes frozen sections (increased positive margins) to limit anesthesia on elderly patient with co-morbidities (longer LOS)

cT1

- LOS did not impact positive margin rate
- LOS > 4 days predicted worse survival

Discussion (cont.)

cT2-3

- LOS > 4 days predicted fewer positive margins
 - Best explained by flap reconstruction since other factors increasing LOS should *increase* positive margins
- LOS > 4 days had no impact on survival
 - Survival benefit from fewer positive margins likely obscured by other factors causing increased LOS decreasing survival

Conclusions

- For patients with cT2-3 tumors, hospital LOS >4 days predicted lower positive margin rates, suggesting that vascularized reconstruction allowed more aggressive oncologic resections
- Similar survival rates despite more co-morbidities suggests a survival benefit resulting from the lower positive margins

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