

Introduction

Oral cancer is the 6th most common type of cancer worldwide, of which >90% consists of squamous cell carcinoma.^{1,2} Surgical resection is the mainstay of definitive treatment for oral cavity squamous cell carcinoma (OCSCC) while radiotherapy and chemotherapy are usually employed as adjuncts.³ Various reconstructive methods are employed to reestablish function and/or aesthetics of the oral cavity after resection. Free tissue transfer offers robust reconstruction with high success rates and improved functional outcomes.⁴⁻⁶ In addition to improved function, flap reconstruction may offer improved oncologic outcomes for patients with advanced OCSCC, perhaps by permitting more extensive resections with negative margins.^{5,7} However, oncologic outcomes after flap reconstruction for *early* OCSCC are not well established. In addition, there is concern that burying the resection cavity with free tissue may delay local recurrence detection compared to healing by secondary intention, primary closure, or graft placement. As a result, the aim of this study was to explore the impact of reconstructive technique on the time to detection of pT1-T3 OCSCC local recurrence.

Methods

We conducted a retrospective cohort study of consecutive patients with primary pT1-T3 OCSCC (AJCC 8th) who underwent surgical resection from January 2000 to October 2017. We excluded patients with pN3 or M1 disease. Zero time was the date of surgery. The endpoints were date of local recurrence or censoring. Reconstructive methods included healing by secondary intention; primary closure; grafts, which included both autologous skin grafts and acellular dermal matrix; and flaps. Flap reconstruction included locoregional and free tissue transfer. Kaplan-Meier and Cox proportional hazards analysis were used to estimate differences in time to local recurrence.

Table 1. Baseline demographic characteristics of the study population.

Variables	No Local Recurrence (n=271)	Local Recurrence (n=44)	Median or Proportional Difference (95% CI)
Age (years), median (range)	70.0 (25-108)	65.0 (34-86)	8.0 (3.0 to 12.0)
Female	119 (43.9%)	18 (40.9%)	3.0% (-12.7% to 18.7%)
Smoking history	149 (55.0%)	31 (70.5%)	-15.5% (-30.2% to -0.8%)
>10 pack years	119 (43.9%)	27 (61.4%)	-17.5% (-33.1% to -1.9%)

Table 2. Baseline general health, tumor, and treatment characteristics of the study population.

Variables	No Local Recurrence (n=271)	Local Recurrence (n=44)	Proportional Difference (95% CI)
Adult Comorbidity Evaluation-27 (ACE-27) ⁸			
None/Mild	160 (65.6%)	18 (41.9%)	23.7% (8.1% to 39.3%)
Moderate/Severe	84 (34.4%)	25 (58.1%)	-23.7% (-39.3% to -8.1%)
T stage			
pT1	169 (62.4%)	16 (36.4%)	26.0% (10.7% to 41.3%)
pT2-T3	102 (37.6%)	28 (63.6%)	-26.0% (-41.3% to -10.7%)
Adjuvant treatment	75 (27.7%)	13 (29.5%)	-1.8% (-16.3% to 12.7%)
Reconstruction			
Secondary	25 (9.2%)	13 (29.5%)	-20.3% (-34.2% to -6.4%)
Primary	74 (27.3%)	8 (18.2%)	9.1% (-3.5% to 21.7%)
Graft	80 (29.5%)	6 (13.6%)	15.9% (4.4% to 27.4%)
Flap	92 (33.9%)	17 (38.6%)	-4.7% (-20.2% to 10.7%)

Results

In total, 315 patients were included, of which 44 subjects (14%) developed local recurrence. The median follow-up time was 43.0 (range 0-196) months. The baseline characteristics of the study population are described (Tables 1-2). The cohort with local recurrence had significantly more smokers, more overall comorbidity burden, and higher T stage. Overall, the time to local recurrence was 9.5 (range 1-59) months.

For reconstruction, 38 (12%) patients underwent secondary intention; 82 (26%), primary closure; 86 (27%), graft coverage; and 109 (35%), flap coverage. The 5-year local recurrence free rates for secondary intention, primary closure, graft reconstruction, and flap reconstruction were 60% (95% CI 42%-77%), 87% (78%-96%), 93% (87%-98%), and 82% (74%-90%), respectively (Figure 1). Patients with and without flap reconstruction had a median time to recurrence of 7.0 (range 1-46) months and 15.0 (1-59) months respectively, equating to a median difference of 13.0 (5.0-22.0) months (Figure 2). Flap reconstruction had a hazard ratio of 0.88 (95% CI 0.42-1.85) (Table 3).

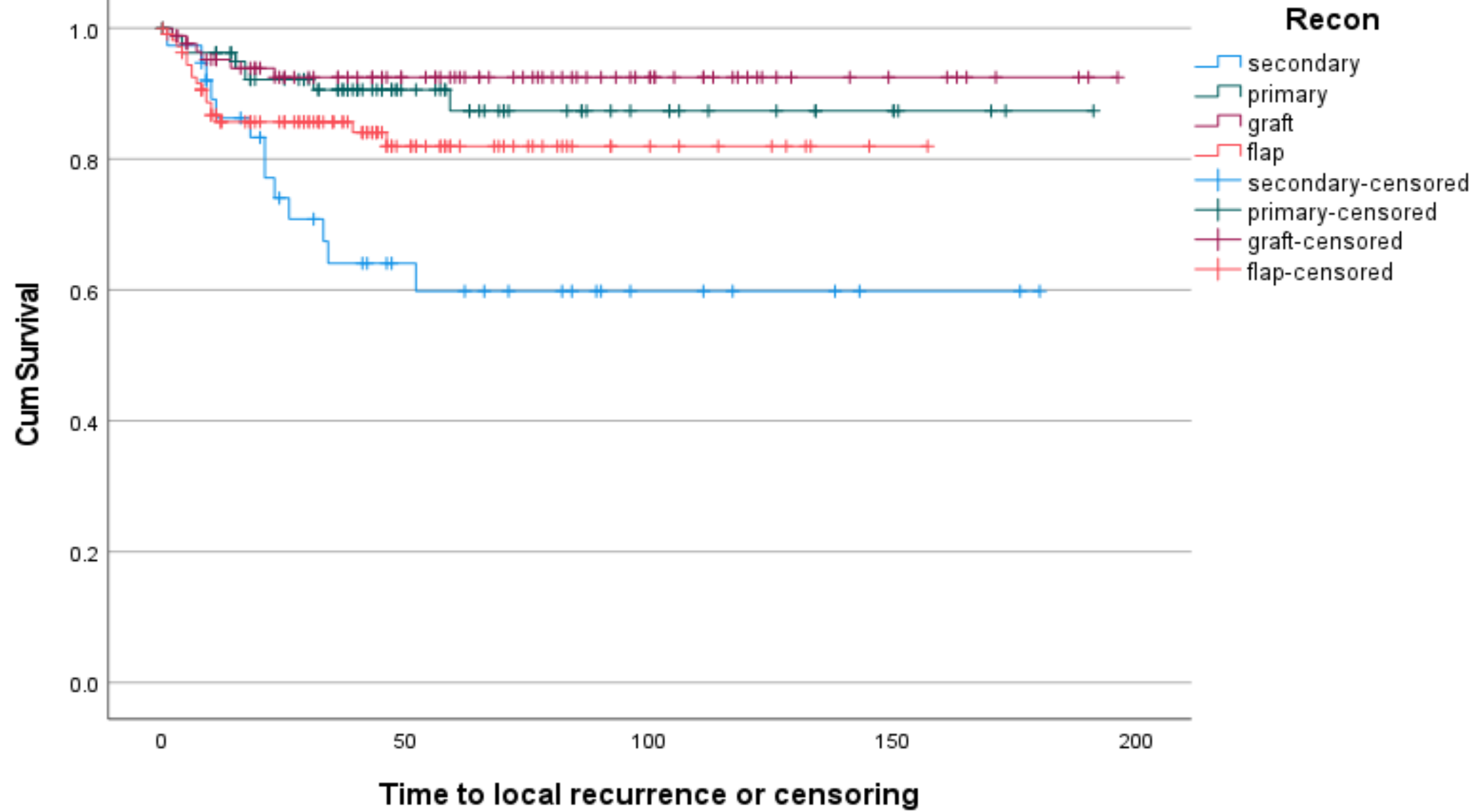


Figure 1. Kaplan-Meier curves of the rate of detecting local recurrence based on reconstructive technique.

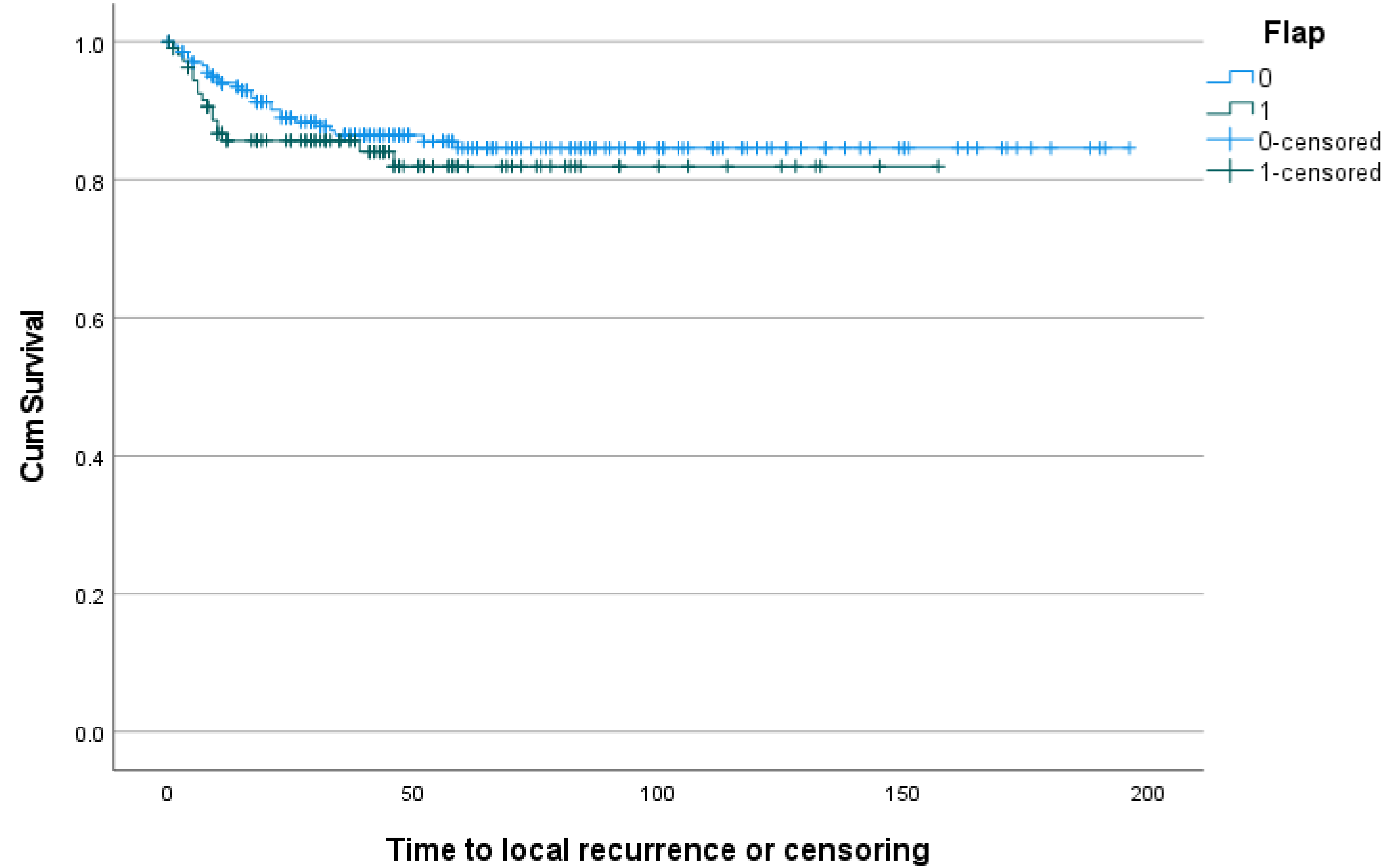


Figure 2. Kaplan-Meier curves of the rate of detecting local recurrence based on defect coverage with a flap for all patients in the cohort.

Results, continued

Other variables associated with decreased recurrence-free survival were >10 pack year smoking history (HR 2.14, 95% CI 1.17-3.93), moderate/severe ACE-27 score (HR 2.75, 95% CI 1.50-5.06), pT2-T3 stage (HR 2.76, 95% CI 1.49-5.10), and perineural invasion (HR 2.01, 95% CI 1.09-3.74). Multivariable analysis revealed no clinically meaningful differences in time to detecting local recurrence between flap reconstruction and other methods of reconstruction after controlling for the presence of these covariates (Table 4).

Table 3. Univariate survival analysis results with reported hazard ratios (HR) for local recurrence.

Variables	HR (95% CI)
Age > 65 years	0.59 (0.32 to 1.06)
Female	0.86 (0.47 to 1.57)
Smoking history	2.07 (1.08 to 3.96)
>10 pack years	2.14 (1.17 to 3.93)
Moderate/severe ACE-27 score	2.75 (1.50 to 5.06)
pT2-T3 stage	2.76 (1.49 to 5.10)
Lymphovascular invasion	1.46 (0.57 to 3.70)
Perineural invasion	2.01 (1.09 to 3.74)
Adjuvant therapy	1.08 (0.56 to 2.06)
Flap reconstruction	0.88 (0.42 to 1.85)

Table 4. Multivariable survival analysis results with adjusted hazard ratios (aHR) for local recurrence.

Variables	aHR (95% CI)
Flap reconstruction	0.84 (0.44 to 1.61)
>10 pack year	1.73 (0.93 to 3.25)
Moderate/severe ACE-27 score	2.32 (1.25 to 4.30)
pT2-T3 stage	2.38 (1.16 to 4.89)
Perineural invasion	1.26 (0.63 to 2.51)

Conclusions

Patients with pT1-T3 OCSCC undergoing flap reconstruction had a shorter median time to recurrence than those who healed by secondary intention, primary closure, or graft placement. After controlling for T stage, smoking history, comorbidity burden, and perineural invasion, there were no differences in time to detection of local recurrence between flap reconstruction and other techniques. These findings suggest that defect coverage does not delay local recurrence detection as planning for flap reconstruction may permit more extensive oncologic resection.

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