When More is Less: Shortcomings of Excisional Biopsy in Early-Stage Oral Cavity Carcinoma

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Introduction

- Incisional biopsy is the most common method of diagnosing oral cavity malignancy.
- Small tumors may be evaluated with excisional biopsy, in which the entire lesion is removed prior to a known diagnosis of malignancy.
- Excisional biopsies are often done at institutions that do not perform the definitive oncologic therapy, and this may limit the availability of pathologic data used to make treatment decisions.
- This effort to simplify may have unintended consequences that impair appropriate management of malignancy at the treating institution.
- The objectives of this study were to:

  1. Compare the quantity/quality of available data about the primary tumor
  2. Compare differences in treatment
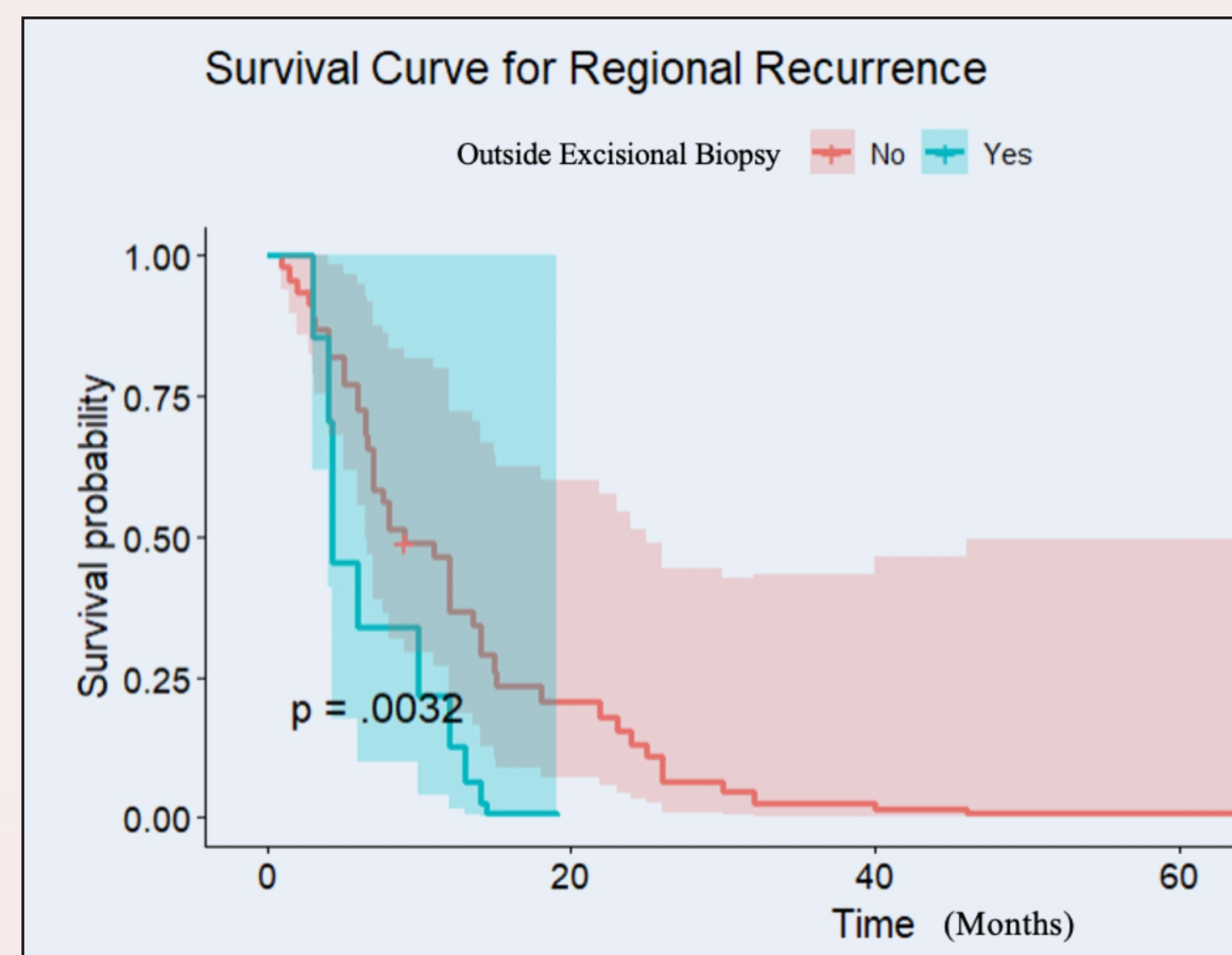 3. Compare differences in local and regional control

Methods

- Retrospective series of adult patients (≥18 years) who underwent primary surgery for clinical T1-T2, N0 oral cavity squamous cell carcinoma between 2003 and 2020 at four tertiary referral centers.
- Patients with distant metastasis or recurrent disease at presentation, history of head and neck radiation or major head and neck surgery were excluded.
- Biopsies were deemed excisional if no visible lesion was present on initial examination and/or if no invasive tumor was present on definitive resection.
- All remaining biopsies were termed incisional.
- Univariable quantitative and qualitative analyses were performed to investigate differences of means and proportions between groups.
- Multivariable Cox proportional hazards models were constructed to investigate the association between local and regional control and associated factors
- Models were isolated to pathologic T1 tumors and were constructed to control for age, smoking status, depth of invasion, perineural invasion, lymphovascular invasion, pathologic N classification, neck dissection, and radiation.
- Factors were iteratively removed from the multivariable models to minimize model AIC.
- P values less than 0.05 were considered statistically significant.

Variable	Total Missing	Excisional	Incisional	P.Value
	N= 720	N= 107	N= 613	
Pathologic T Classification	25 (3.47%)	12 (11.21%)	13 (2.12%)	<0.001
1st Dimension	25 (3.47%)	12 (11.21%)	13 (2.12%)	<0.001
2nd Dimension	363 (50.42%)	72 (67.29%)	291 (47.47%)	<0.001
Depth of Invasion	63 (8.75%)	15 (14.02%)	48 (7.83%)	<0.001
Tumor Grade	27 (3.75%)	13 (12.15%)	14 (2.28%)	0.2596
Closest Margin	197 (27.36%)	38 (35.51%)	159 (25.94%)	0.4753
Perineural Invasion	25 (3.47%)	9 (8.41%)	16 (2.61%)	0.0017
Lymphovascular Invasion	27 (3.75%)	10 (9.35%)	17 (2.77%)	<0.001
Mean missing	1.01	1.59	0.93	<0.001

Table 1: Missing Data in both excision and incisional biopsy groups.

Regional Recurrence	Hazard Ratio	p.value	Confidence Interval	Standard error	Statistics
Outside Excisional Biopsy	3.4898	0.0032	1.52-8.02	0.42	2.95
Age	1.0129	0.2061	0.99-1.03	0.01	1.26
Active Smoker	0.5483	0.068	0.29-1.05	0.33	-1.83
Depth Of Invasion	1.1015	0.0134	1.02-1.19	0.04	2.47
Local Recurrence					
Outside Excisional Biopsy	0.4577	0.0644	0.20-1.05	0.42	-1.85
Age	1.0162	0.0706	1.00-1.03	0.01	1.81
Active Smoker	0.7287	0.3571	0.37-1.43	0.34	-0.92
Depth Of Invasion	1.1455	0.002	1.05-1.25	0.04	3.1

Table 2: Cox-proportional Hazard model for regional and local recurrent in incisional vs excisional biopsies.

Figure 1: Cox proportional hazard model for adjusted risk of regional recurrence based on outside excisional biopsy status.

Results

- 720 patients were included (mean age 61.9, 54.4% male, 92.5% white, 63.6% with history of smoking, mean (SD) follow-up 57.1 months (43.1)).
- Outside excisional biopsy was performed in 107 cases (14.9%).
- All patients with excisional biopsies underwent re-resections at the tertiary referral centers.
- Patients undergoing outside excisional biopsies did not differ in sex or race, were slightly younger (58.8 vs 62.4, p=0.016) and with lower BMI (29.1 vs 27.3, p=0.004).
- Among patients with outside excisional biopsies, 76 had residual invasive tumor or high-grade dysplasia on re-resection (71.0%).
- Patients with outside excisional biopsies had higher proportions of pathologic T1 tumors (90% vs 71.6%, p<0.001), smaller mean greatest tumor dimension (7.5mm vs 13.4mm, p=0.001), lower depth of invasion (3.5mm vs 6.0mm, p=0.016).
- Among eight pathologic details considered relevant to the primary tumor (Tclassification, greatest tumor dimension, depth of invasion/tumor thickness, histologic grade, perineural invasion, lymphovascular invasion, and distance from closest margin), patients with outside excisional biopsies had more missing variables per patient relative to other biopsy types (1.59 vs 0.90, p<0.001, table 1)
- Patients with outside excisional biopsies had lower rates of neck dissection (52.3% vs 73.6%, p<0.001) and radiotherapy (14.2% vs 26.4%, p=0.007) compared to other biopsy types.
- When controlling for age, smoking status, depth of invasion, perineural invasion, and radiation, patients who underwent outside excisional biopsy had lower rates of regional control (HR 3.49, CI 1.52-8.02, p=0.0032, table 2).
- Local control did not differ between groups on multivariable analysis (table 2).

Conclusion

- Oral cavity tumors evaluated by excisional biopsy represent a generally favorable subgroup with small tumor size and shallow depth of invasion.
- Excisional biopsy is likely performed to avoid a false negative biopsy and to simplify treatment by combining diagnostic and therapeutic procedures.
- Excisional biopsy on average provides less pathologic data for which treatment decisions can be made.
- In the absence of such data, physicians may tend to assume favorable pathologic features and, in some cases, may undertreat patients.
- This is evident in the lower rates of neck dissection and radiotherapy and the higher rates of regional recurrence in multivariable analysis.
- The data in this study provides support for incisional biopsy being considered the standard of care for initial assessment of oral cavity lesions.

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