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ORIGINAL RESEARCH

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Factors associated with total laryngectomy following organ-preserving treatment of laryngeal SCC

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Abstract

Objective(s): A subset of laryngeal squamous cell carcinoma (LSCC) patients undergoing larynx preserving treatment ultimately require total laryngectomy (TL) for oncologic or functional reasons. This study aims to identify TL risk factors in these patients.

Methods: Retrospective cohort study using Veterans Affairs (VA) database. T1–T4 LSCC cases treated with primary radiotherapy (XRT) or chemoradiotherapy (CRT) were assessed for TL and recurrence. Binary logistic and Cox regression and Kaplan–Meier analyses were implemented.

Results: Of 5390 cases, 863 (16.0%) underwent TL. On multivariable analysis, age (adjusted odds ratio: 0.97 [0.96–0.98]; $p < .001$) and N3 disease (0.42 [0.18–1.00]; $p = .050$) were associated with reduced risk of TL, whereas current alcohol use (1.22 [1.04–1.43]; $p = .015$) and >T1 disease (T2, 1.76 [1.44–2.17]; $p < .001$; T3, 2.06 [1.58–2.68]; $p < .001$; T4, 1.79 [1.26–2.53]; $p = .001$) were associated with increased risk of TL. However, N2 (adjusted hazard ratio: 1.30 [1.10–1.55]; $p = .003$) and N3 (2.02 [1.25–3.26]; $p = .004$) disease were associated with an increased risk for local recurrence. Compared to XRT, treatment with CRT was associated with reduced risk for local recurrence after adjusting for other factors (0.84 [0.70–0.99]; $p = .044$). Those who do not receive TL following local recurrence have poorer disease-specific survival (log-rank, $p < .001$). In patients without local recurrence, N2 disease was associated with a fourfold increase in risk of TL (4.24 [1.83–9.82]; $p < .001$).

This study was presented at the American Head and Neck Society Annual Meeting on July 12, 2023 in Montreal, QC, Canada.

Conclusion: Advanced nodal stage was associated with reduced rates of salvage TL in the setting of local recurrence, and subsequent worse prognosis after recurrence. Conversely, advanced nodal stage may increase the risk for functional salvage TL in patients without recurrence.

Level of Evidence: Level 3.

KEYWORDS

laryngeal squamous cell carcinoma, larynx preservation, salvage laryngectomy, recurrence, Veterans Affairs

1 | INTRODUCTION

The Veterans Affairs (VA) study, published in 1991, provided some of the first randomized data to support the treatment of laryngeal squamous cell carcinoma (LSCC) with a combination of chemotherapy and radiation rather than laryngectomy.[1] Subsequently, Forastiere et al. demonstrated that in locally advanced LSCC, concurrent chemoradiotherapy (CRT) delivered superior locoregional control and laryngectomy-free survival compared to induction chemotherapy with radiation or radiation alone (XRT).[2]

Nevertheless, in practice, an estimated 16%–36% of patients with advanced LSCC treated with laryngeal preservation (LP) will ultimately receive a total laryngectomy (TL), either for local disease recurrence or functional indications, underscoring the need for identification of risk factors for TL following LP.[3–7] To date, few clinical features have been associated with TL following curative-intent treatment with LP in patients with moderately advanced LSCC.[8] LP is often favored for possibility of voice and speech retention without permanent stoma along with improved quality of life.[9,10] However, LSCC patients treated with LP may experience high-grade dysphagia, aspiration, and need for future tracheostomy.[11] T4 patients are at particularly high risk, and some literature supports the use of primary laryngectomy in these patients over CRT/XRT.[11,12] In post-CRT LSCC patients undergoing surgical salvage, the rate of major complications is as high as 54%.[13] Therefore, it is essential for providers to identify patients with risk factors for salvage TL following initial LP to inform shared decision-making and guide treatment.

In this study, we aimed to use a VA database to identify risk factors for receipt of salvage TL following larynx-preserving treatment in patients with LSCC.

2 | MATERIALS AND METHODS

Previously published data from the VA national database were interrogated with approval by the Research and Development Committee of the VA San Diego Healthcare System.[14–16] Inclusion criteria were LSCC, T category ≥1 to include early and advanced disease, and initial nonsurgical definitive treatment with either primary CRT or XRT. Exclusion criteria were in situ disease, distant metastases at diagnosis, missing staging or treatment information, or age under 18. For TNM staging, cases were coded using the *AJCC 8th edition Cancer Staging Manual*.[17] Pathological staging data superseded clinical staging data when available. All reported staging data refers to the original disease stage as opposed to that at recurrence. Anatomic subsite was discretely coded as either "glottis," "supraglottis," "subglottis," "larynx, NOS," or "larynx, overlapping."

Clinical, demographic, and treatment variables were compared between cases that received TL (TL+) and those that did not (TL−) using descriptive statistics (chi-squared for categorical variables and two-sided *T* test or Mann–Whitney test for continuous variables). Univariable and multivariable binary logistic regression models were generated to identify factors associated with receipt of TL following definitive nonsurgical treatment. Similarly, Cox proportional hazards regression models were generated to identify factors associated with local recurrence, defined as recurrence at the larynx or tissue adjacent to the primary tumor site. Time to local recurrence was set as the time between date of diagnosis and date of local recurrence. Cases were censored at time of either last contact or death. For regression analyses, covariates with $p < .100$ on univariable analysis were included in a multivariable model generated using a backward conditional method whereby variables with $p > .100$ were removed at each step. Furthermore, Kaplan–Meier analyses and log-rank tests were performed to analyze differences in overall survival based on receipt of TL. All analyses were performed using IBM SPSS Statistics v.29.0.2.0.[18]

3 | RESULTS

3.1 | Analysis of risk factors for salvage TL in a VA database

A total of 5390 patients from the VA database met inclusion criteria. Of those, 863 (16.0%) received subsequent TL (Table 1). Mean age at diagnosis was 63.0 years in TL+ cases versus 65.7 in TL− cases (two-sided *T* test, $p < .001$). The median duration of follow-up among all cases was 3.0 years (interquartile range: 1.3–5.8) and did not vary by receipt of TL (independent samples median test, $p = .366$). Of the patients who received TL, 96.8% had local disease recurrence. Among cases with local recurrence, rates of distant recurrence did not differ

TABLE 1 Demographic and clinical characteristics of patients treated with organ preservation.

	n (%) 5390 (100)	TL+ 863 (16.0)	TL− 4527 (84.0)	*p*
Age at diagnosis, mean (SD)	65.3 (9.0)	63.0 (8.3)	65.7 (9.1)	**<.001**
Length of follow up, median, years [IQR]	3.0 [1.3–5.8]	3.1 [1.6–5.8]	2.9 [1.2–5.8]	.366
Sex				
Male	5339 (99.1)	858 (99.5)	4481 (99.0)	.146
Female	48 (0.9)	4 (0.5)	44 (1.0)	
Race				
White	4210 (79.0)	672 (78.0)	3538 (79.1)	.116
Black	1075 (20.2)	186 (21.6)	889 (19.9)	
Other	46 (0.9)	3 (0.3)	43 (1.0)	
Charlson–Deyo score				
0	2049 (38.1)	355 (41.1)	1694 (37.4)	.110
1	670 (12.4)	98 (11.4)	572 (12.6)	
≥2	2668 (49.5)	410 (47.5)	2258 (49.9)	
Tobacco history				
Past/never	2150 (39.9)	317 (36.7)	1833 (40.5)	**.039**
Current	3240 (60.1)	546 (63.3)	2694 (59.5)	
Alcohol history				
Past/never	2409 (51.0)	339 (44.8)	2070 (52.2)	**<.001**
Current	2313 (49.0)	417 (55.2)	1896 (47.8)	
Primary site				
Glottis	3229 (59.9)	502 (58.2)	2727 (60.2)	.330
Supraglottis	1776 (32.9)	286 (33.1)	1490 (32.9)	
Subglottis	57 (1.1)	12 (1.4)	45 (1.0)	
Larynx, NOS	235 (4.4)	43 (5.0)	192 (4.2)	
Larynx, overlapping	93 (1.7)	20 (2.3)	73 (1.6)	
T category				
1	2089 (38.8)	249 (28.9)	1840 (40.6)	**<.001**
2	1627 (30.2)	300 (34.8)	1327 (29.3)	
3	1238 (23.0)	238 (27.6)	1000 (22.1)	
4	436 (8.1)	76 (8.8)	360 (8.0)	
N category				
0	3965 (73.6)	632 (73.2)	3333 (73.6)	.261
1	365 (6.8)	64 (7.4)	301 (6.6)	
2	987 (18.3)	161 (18.7)	826 (18.2)	
3	73 (1.4)	6 (0.7)	67 (1.5)	
Stage				
1	2119 (39.3)	262 (30.4)	1857 (41.0)	**<.001**
2	1175 (21.8)	233 (27.0)	942 (20.8)	
3	817 (15.2)	152 (17.6)	665 (14.7)	
4A	1206 (22.4)	210 (24.3)	996 (22.0)	
4B	73 (1.4)	6 (0.7)	67 (1.5)	
Treatment modality				
XRT	3299 (61.2)	496 (57.5)	2803 (61.9)	**.014**
CRT	2091 (38.8)	367 (42.5)	1724 (38.1)	

(Continues)

TABLE 1 (Continued)

	n (%) 5390 (100)	TL+ 863 (16.0)	TL− 4527 (84.0)	*p*
Any recurrence				
Yes	1380 (25.6)	863 (100)	517 (11.4)	**<.001**
No	4010 (74.4)	0 (0.0)	4010 (88.6)	
Local recurrence				
Yes	1300 (24.1)	835 (96.8)	465 (10.3)	**<.001**
No	4090 (75.9)	28 (3.2)	4062 (89.7)	
Regional recurrence				
Yes	190 (3.5)	123 (14.3)	67 (1.5)	**<.001**
No	5200 (96.5)	740 (85.7)	4460 (98.5)	
Distant recurrence				
Yes	33 (0.6)	14 (1.6)	19 (0.4)	**<.001**
No	5357 (99.4)	894 (98.4)	4508 (99.6)	

Bolded values are *p* values <0.05, denoting significance.
Abbreviations: CRT, chemoradiotherapy; IQR, interquartile range; TL, total laryngectomy; XRT, radiotherapy.

by receipt of TL (1.2% vs. 1.5%, χ^2 $p = .640$), whereas regional recurrence was more common in TL+ cases (11.7% vs. 4.5%, $p < .001$).

Age (adjusted odds ratio [aOR]: 0.97 [0.96–0.98]; $p < .001$) and N3 disease (0.42 [0.18–1.00]; $p = .050$) were associated with a reduced risk for TL after adjusting for alcohol history, T category, and treatment modality (Table 2). Primary treatment modality of CRT trended toward an associated with reduced risk for receipt of TL ($p = .073$) after adjusting for other factors. Current alcohol use (1.22 [1.04–1.43]; $p = .015$) was associated with increased risk for TL on multivariable analysis, as was T category >T1 (T2, 1.76 [1.44–2.17]; $p < .001$; T3, 2.06 [1.58–2.68]; $p < .001$; T4, 1.79 [1.26–2.53]; $p = .001$).

3.2 | Factors associated with local recurrence

Given that 96% of patients who received TL experienced local recurrence, we then performed Cox regression analyses to assess for factors associated with local recurrence. Local disease recurrence occurred in 24.1% of all cases. Compared to T1 disease, T2 (adjusted hazard ratio [aHR]: 1.69 [1.45–1.98]; $p < .001$), T3 (1.94 [1.58–2.37]; $p < .001$), and T4 (2.25 [1.75–2.90]; $p < .001$) disease were each independently associated with increased risk of local recurrence after adjusting for age, race, N category, and treatment modality (Table 3; Figure 1A). Median times from diagnosis to local recurrence in T1–T4 patients were: 15, 13, 12, and 11 months, respectively ($p < .001$, independent samples median test). Compared to N0 disease, N2 (1.30 [1.10–1.55]; $p = .003$) and N3 (2.02 [1.25–3.26]; $p = .004$) disease were also associated with increased risk for local recurrence on multivariable analysis (Figure 1B). Median times to local recurrence in N0-N3 patients were: 14, 12, 12, and 7 months, respectively ($p < .001$, independent samples median test). After adjusting for disease stage, age, and race, CRT was also associated with decreased risk for local recurrence compared to XRT (aHR: 0.84 [0.70–0.99]; $p = .044$).

3.3 | Salvage laryngectomy following local recurrence versus non-oncologic laryngectomy

Given that N2–3 disease was associated with increased risk of local recurrence but decreased risk of TL, we separately investigated receipt of TL in patients with or without local recurrence to distinguish between true salvage laryngectomy and laryngectomy for non-oncologic indications (i.e., functional TL). Local recurrence occurred in 96.8% of TL+ patients, whereas the remaining 3.2% of TL+ patients received TL for nononcologic indications. In N0 cases with local recurrence, 6.5% had concurrent regional recurrence, compared to 14.4% of N1 cases, 15.5% of N2 cases, and 21.1% of N3 cases (χ^2, $p < .001$). Rates of distant recurrence only differed significantly between N1 (4.1%) and N0 (0.9%) cases ($p = .043$). Among patients with local recurrence, rates of distant recurrence were not significantly greater in TL− patients compared to TL+ patients, regardless of N stage (N0, 1.0% [TL−] vs. 0.8% [TL+]; N1, 5.9 vs. 3.2; N2, 1.6 vs. 2.0; N3, 0.0 vs. 0.0; χ^2, $p > .5$ for each comparison).

In those with local recurrence, T category was again associated with increased odds of salvage TL and N category was associated with reduced odds of TL, after adjusting for age, alcohol history, and treatment modality (Table 4). Of N2 and N3 cases with local recurrence, 54.2% and 26.3% each received TL, in comparison to 67.9% of N0 cases with recurrence. Notably, patients with local recurrence who did not receive salvage TL experienced worse overall survival compared to those who received salvage TL surgery (log-rank, $p < .001$, Figure 2). Concordantly, patients with advanced nodal disease experienced worse survival following local recurrence (log-rank, $p < .001$, Supplemental Figure 1).

TABLE 2 Binary logistic regression, factors associated with total laryngectomy amongst cases treated with CRT or XRT.

	n = 5390	Univariate OR (95% CI)	*p*	Multivariate aOR[a] (95% CI)	*p*
Age at diagnosis	5390	0.97 (0.96–0.97)	**<.001**	0.97 (0.96–0.98)	**<.001**
Sex, *n*					
Male	5339	Ref	-		
Female	48	0.48 (0.17–1.33)	.155		
Race, *n* (%)					
White	4210	Ref	-		
Black	1075	1.10 (0.92–1.32)	.288		
Other	46	0.37 (0.11–1.19)	.094		
Charlson–Deyo score					
0	2049	Ref	-		
1	670	0.82 (0.64–1.04)	.104		
≥2	2668	0.87 (0.74–1.01)	.071		
Tobacco history					
Past/never	2150	Ref	-		
Current	3240	1.17 (1.01–1.36)	**.039**		
Alcohol history					
Past/never	2409	Ref	-	Ref	-
Current	2313	1.34 (1.15–1.57)	**<.001**	1.22 (1.04–1.43)	**.015**
Primary site					
Glottis	3229	Ref	-		
Supraglottis	1776	1.04 (0.89–1.22)	.605		
Subglottis	57	1.45 (0.76–2.76)	.259		
Larynx, NOS	235	1.22 (0.86–1.72)	.264		
Larynx, overlapping	93	1.49 (0.90–2.46)	.122		
T category					
1	2089	Ref	-	Ref	-
2	1627	1.67 (1.39–2.01)	**<.001**	1.76 (1.44–2.17)	**<.001**
3	1238	1.76 (1.45–2.13)	**<.001**	2.06 (1.58–2.68)	**<.001**
4	436	1.56 (1.18–2.07)	**.002**	1.79 (1.26–2.53)	**.001**
N category					
0	3965	Ref	-	Ref	-
1	365	1.12 (0.85–1.49)	.428	0.89 (0.65–1.23)	.483
2	987	1.03 (0.85–1.24)	.775	0.80 (0.63–1.01)	.058
3	73	0.47 (0.20–1.09)	.080	0.42 (0.18–1.00)	**.050**
Treatment modality				0	
XRT	3299	Ref	-	Ref	-
CRT	2091	1.20 (1.04–1.39)	**.014**	0.81 (0.65–1.02)	.073

Bolded values are *p* values <0.05, denoting significance.
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CRT, chemoradiotherapy; OR, odds ratio; XRT, radiotherapy.
[a]Adjusted for age, alcohol history, T category, N category, and treatment modality.

In patients without local recurrence, N2 disease was associated with increased risk for TL compared to N0 disease (4.24 [1.83–9.82]; $p < .001$). Neither T category, age, nor treatment modality was associated with TL after adjusting for N category. Of the 4090 cases that did not experience local recurrence, 28 were reported to receive TL within the follow-up period (0.7%).

4 | DISCUSSION

In this study of LSCC patients treated with LP, advanced nodal disease was found to be independently associated with reduced rates of salvage TL despite an increased rate of local recurrence. The discrepancy between rates of salvage TL and local recurrence in

TABLE 3 Cox regression for factors predictive of time to local disease recurrence in XRT and CRT cases.

	$n = 5390$	Univariate HR (95% CI)	p	Multivariate aHR[a] (95% CI)	p
Age at diagnosis, years, mean (SD)	5390	0.98 (0.97–0.99)	**<.001**	0.99 (0.98–0.99)	**<.001**
Sex					
Male	5313	Ref	-		
Female	48	0.53 (0.24–1.17)	.116		
Race					
White	4191	Ref	-	Ref	-
Black	1069	1.14 (0.99–1.30)	.061	1.09 (0.94–1.26)	.241
Other	46	0.47 (0.20–1.14)	.096	0.43 (0.16–1.14)	.090
Charlson–Deyo score					
0	2036	Ref	-		
1	667	0.86 (0.72–1.04)	.117		
≥2	2658	0.91 (0.81–1.02)	.114		
Tobacco history					
Past/never	2139	Ref	-		
Current	3225	1.13 (1.01–1.26)	**.037**		
Alcohol history					
Past/never	2395	Ref	-		
Current	2305	1.12 (1.00–1.26)	.055		
Primary site					
Glottis	3210	Ref	-		
Supraglottis	1769	1.28 (1.14–1.44)	**<.001**		
Subglottis	57	1.38 (0.87–2.21)	.175		
Larynx, NOS	235	1.45 (1.12–1.88)	**.005**		
Larynx, overlapping	93	1.50 (1.03–2.19)	**.036**		
T category					
1	2075	Ref	-	Ref	-
2	1620	1.71 (1.49–1.95)	**<.001**	1.69 (1.45–1.98)	**<.001**
3	1234	1.91 (1.65–2.21)	**<.001**	1.94 (1.58–2.37)	**<.001**
4	435	2.36 (1.93–2.89)	**<.001**	2.25 (1.75–2.90)	**<.001**
N category					
0	3942	Ref	-		
1	364	1.39 (1.12–1.71)	**.002**	1.10 (0.86–1.40)	.449
2	985	1.59 (1.37–1.80)	**<.001**	1.30 (1.10–1.55)	**.003**
3	73	2.35 (1.49–3.70)	**<.001**	2.02 (1.25–3.26)	**.004**
Treatment modality					
XRT	3281	Ref	-	Ref	-
CRT	2083	1.47 (1.31–1.64)	**<.001**	0.84 (0.70–0.99)	**.044**

Bolded values are p values <0.05, denoting significance.
Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; CRT, chemoradiotherapy; HR, hazard ratio; XRT, radiotherapy.
[a]Adjusted for age, race, T category, N category, and treatment modality.

patients with advanced nodal disease highlights the risk for aggressive recurrent disease, which may not be amenable to surgical salvage at the time of recurrence. As has been previously reported advanced T category was associated with increased risk for both local recurrence and subsequent salvage TL. In patients without local recurrence, advanced nodal stage was associated with receipt of TL.

Nodal disease is well known to portend poor prognosis in laryngeal cancer. Within this VA database cohort, 47.6% of laryngeal cancer patients with advanced nodal disease did not receive salvage

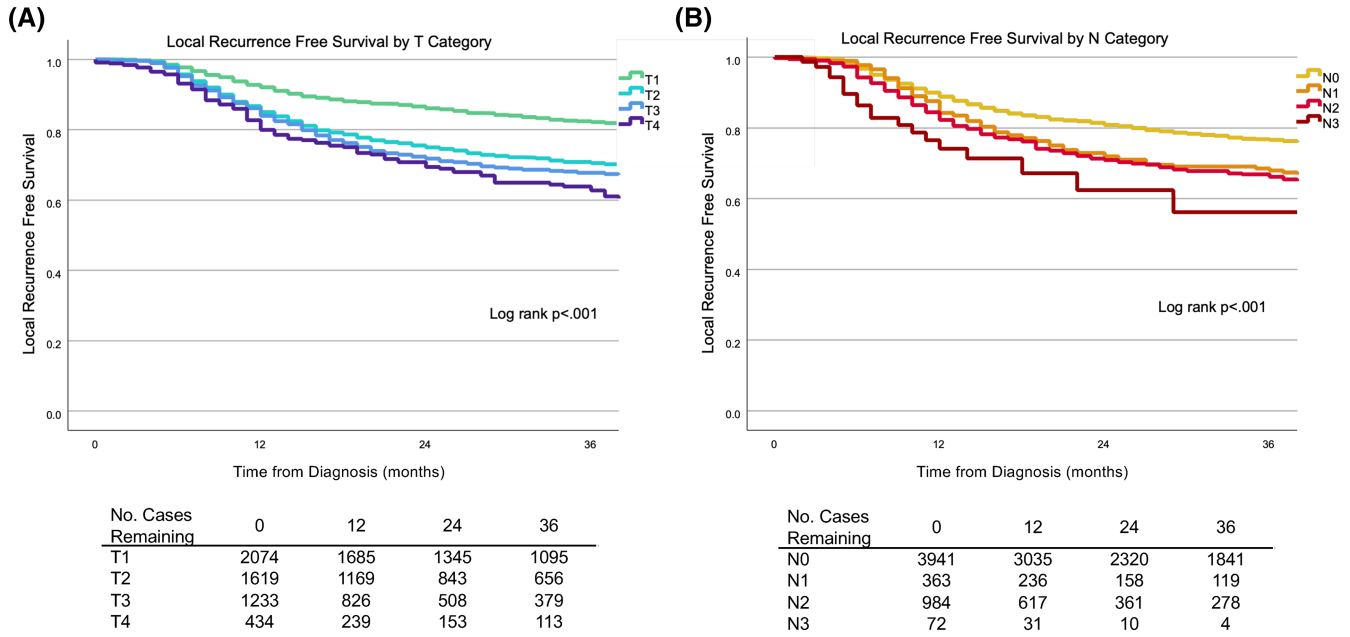


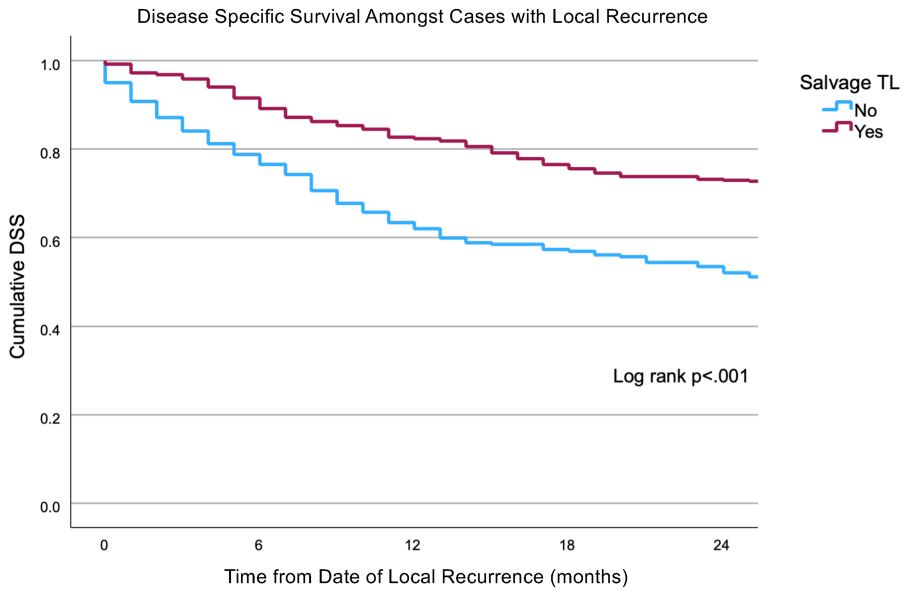
FIGURE 1 Local disease recurrence by (A) T category and (B) N category at time of diagnosis.

TABLE 4 Binary logistic regression, factors associated with total laryngectomy (TL) based on local recurrence.

Local recurrence	Yes (salvage TL)		No (functional TL)	
	aOR[a] (95% CI)	*p*	OR (95% CI)	*p*
Age at diagnosis	0.99 (0.97–1.00)	.066		
Alcohol history				
Past/never	Ref	-		
Current	1.48 (1.15–1.90)	**.002**		
T category				
1	Ref	-		
2	1.46 (1.06–2.03)	**.023**		
3	2.16 (1.41–3.30)	**<.001**		
4	1.38 (0.82–2.31)	.222		
N category				
0	Ref	-	Ref	-
1	0.84 (0.51–1.41)	.516	1.01 (0.13–7.85)	.993
2	0.50 (0.35–0.72)	**<.001**	4.24 (1.83–9.82)	**<.001**
3	0.20 (0.07–0.60)	**.004**	4.90 (0.62–38.70)	.132
Treatment modality				
XRT	Ref	-		
CRT	0.72 (0.50–1.03)	.074		

Bolded values are *p* values <0.05, denoting significance.
Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CRT, chemoradiotherapy; OR, odds ratio; XRT, radiotherapy.
[a]Adjusted for age, alcohol history, T category, N category, and treatment modality.

surgery despite the presence of local recurrence. The specific reasons that patients did not receive salvage laryngectomy for local recurrence were not available for analysis; however, rates of distant disease were not higher in the non-laryngectomy cohort. Other factors, including resectability of locoregional disease recurrence, patient acceptance, and extent of prior treatment toxicity, were not able to be evaluated within this database and could contribute to the lower rates of salvage laryngectomy. Patients who initially present with advanced nodal



No. Cases Remaining	0	6	12	18	24
TL+	775	616	497	402	345
TL-	456	294	191	146	117

FIGURE 2 Disease-specific survival amongst cases with local recurrence based on receipt of salvage TL. TL, total laryngectomy.

disease in laryngeal cancer may also have other factors precluding early diagnosis of disease that make them poor salvage surgery candidates such as medical comorbidities or lack of social support.

In all patients who undergo salvage laryngectomy, complication rates are high.[19] Incidence of pharyngocutaneous fistula following salvage TL is between 21.7% and 28.9%, and rate of any complication may be as high as 67.5%.[4,20] However, primary CRT has been shown to independently predict local complications and pharyngocutaneous fistula following TL when compared to either primary TL or primary XRT.[21] Furthermore, multiple authors report increased postoperative complications in patients who undergo salvage surgery closer to completion of CRT or XRT, potentially due to poorer nutritional and immune status.[19,21,22] Here, we also demonstrate that advanced nodal disease at diagnosis is associated with decreased time to local recurrence following organ-preserving treatment, providing additional rationale for why providers may be less likely to offer these patients salvage laryngectomy following recurrence.

A small minority of patients without local recurrence received TL for nononcologic indications. Functional laryngectomies may be performed to improve patient quality of life in the absence of recurrent disease including chronic aspiration, dyspnea, and dysphagia.[7,23] In those without local recurrence, N2 category was associated with a four-fold increased risk for TL; N3 disease has demonstrated a similar risk for TL, but this was likely underpowered within few cases of functional TL in this cohort. It is well-established that radiation dose and volume to the larynx and adjacent tissues influence functional outcomes such as speech and swallow.[23,24] Patients with advanced nodal disease receive more aggressive treatment and wider neck radiation fields that likely contribute to worse functional outcomes, that may ultimately necessitate TL for nononcologic reasons. In RTOG 91–11, 5% of TLs following organ-preservation treatment were for either "laryngeal dysfunction" or "necrosis," comparable to the 3.2% of patients in this study who received TL for nononcologic indications.[4]

Tobacco and alcohol history are important prognostic factors for survival in head and neck cancer.[25–27] Herein, we report that current alcohol, but not tobacco use, increases the risk of salvage TL in these patients, though neither risk factor was significantly associated with local recurrence after adjusting for disease stage. In contrast, Colasanto et al. report that heavy tobacco uses, and not alcohol use, correlate with local recurrence in LSCC treated with primary XRT.[28] Our study is limited by its dichotomization of both alcohol and tobacco use, which precludes a more granular analysis.

The presented risk factors for TL following initial LP treatment may assist in patient education and decision-making. Receipt of TL after larynx preservation treatment is influenced by risk for local recurrence as well as factors at the time of recurrence that determine whether salvage laryngectomy is ultimately performed. In RTOG 91–11, concurrent CRT significantly improved larynx preservation compared to induction chemotherapy with radiation or radiation alone.[4] In this study, the VA database also recapitulates strong trends between CRT and reduced risk for salvage TL and local recurrence. However, patients with advanced nodal disease may be at risk for unresectable recurrences either due to tumors or patient factors.[4,29,30]

Ultimately, patients with advanced nodal disease are at higher risk for local recurrence and experience lower rates of salvage TL, resulting in decreased cancer-related survival after recurrence. Future studies may examine the factors contributing to reasons that salvage laryngectomy are not performed in the setting of local recurrence which contribute to significantly worse survival, particularly in laryngeal cancer patients with advanced nodal disease.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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