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ORIGINAL ARTICLE

Predictors of Survival in Early-stage Laryngeal Cancer by Treatment Modality

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ABSTRACT

Aim: Our investigation attempts to identify factors associated with improved survival for early-stage laryngeal cancer based on primary therapy using the National Cancer Database (NCDB).

Materials and methods: This is a retrospective cohort with data abstracted from the NCDB. Patients with T1 or T2N0M0 laryngeal cancer from 1998 to 2011 who received radiation only, laser surgery, or laser surgery with adjuvant radiation were included. Chi-square analysis was used to assess and investigate the association between treatment and factors. Overall survival (OS) was assessed via Kaplan–Meier method. Log-rank methods were used to determine factors significant for survival, and a multivariable Cox regression model was performed.

Results: There were 14,276 patients from the NCDB eligible for this study. The majority (91.2%) of patients received primary radiation, 4.7% laser resection, and 4.0% laser resection with radiation. Five-year survival for laser surgery was 78.8% [95% confidence interval (CI) 75.5–82.1%] *vs* 67.2% (95% CI 66.4–68.1%) for radiation alone. Multivariate analysis demonstrated advanced age, increased comorbidities, public or uninsured, T2 stage, supraglottic subsite to be independently associated with worse survival. Treatment with laser only and laser with adjuvant radiation demonstrated a hazard ratio of 0.77 ($p = 0.055$) and 0.65 ($p = 0.001$) when compared with primary radiation.

Conclusion and clinical significance: Survival analysis on early-stage glottic patients in the NCDB showed multiple factors to be independently associated with survival. Outcomes based on treatment suggest an improved survival when utilizing endoscopic surgery as the primary treatment modality.

Keywords: Early stage laryngeal cancer, Survival outcomes, Transoral laser, Treatment.

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INTRODUCTION

Laryngeal cancer was historically treated with primary surgery for early- and advanced stage disease. As the external beam radiation (XRT) techniques advanced, the trend shifted toward the majority of early-stage laryngeal cancer being managed with XRT in the USA, especially after the publishing of the Veterans Affair (VA) Laryngeal Study in 1991. However, with the advent of transoral laser microsurgery (TLM), there has been resurgence in surgical management of early-stage laryngeal cancer.[1] The reported rates of local control with primary surgery for laryngeal cancer *vs* XRT are very comparable (85–100% *vs* 84–95% respectively), although these data are largely based on level III and IV evidence.[2,3] There has been thus far only one randomized trial comparing radiation therapy (RT) and surgery for early-stage laryngeal cancer, which was noted to have some flawed methodology based on a Cochrane review of the topic.[4,5] However, in that study of 234 patients, for T1 tumors, the 5-year disease-free survival (DFS) rate was 71.1% following radiotherapy and 100.0% following open surgery. For the T2 tumors, 60.1% following radiotherapy and 78.7% following surgery, with only the comparison between T2 tumors reaching statistical significance ($p = 0.036$).[4]

Transoral laser microsurgery has largely replaced open surgery in the recent surgical era. The postoperative morbidity is lower with TLM than that with open conservation surgery with comparable oncologic outcomes.[6] The technique often obviates the need for alternative alimentation, tracheostomy, multiple outpatient visits, and prolonged inpatient hospital stay, thereby making it more cost-effective than both open surgery and radiation.[7,8] The existing literature remains controversial on the management of tumors that are T1, T1a, T1b with anterior commissure (AC) involvement, and T2 tumors with regards to TLM *vs* XRT for primary treatment.[2,3,5] In terms of quality of life and voice outcomes, level III evidence has shown some equivocal results and others with improved outcomes of one modality over the other.[9-18] One argument is that TLM allows more accurate, pathologically based staging of the tumor, especially in T2 tumors, which can result in higher larynx preservation rates.[15,16] Not all T2 tumors are created equal; those with deep extension into the paraglottic space have significantly worse local control, and thus may benefit from multimodality treatment.[19,20] Also, the ability to retreat the larynx in a conservative manner if there is tumor recurrence, by either repeat TLM or definitive XRT, is another cited advantage.[7] The purpose of our investigation was to utilize the National Cancer Database (NCDB) to identify factors associated with improved survival for early-stage laryngeal cancer based on the primary treatment modality: Laser resection with or without adjuvant therapy *vs* primary radiation.

MATERIALS AND METHODS

In accordance with Louisiana State University (LSU) guidelines (based on the US Code of Federal Regulations for the Protection of Human Subjects), LSU Health Shreveport Institutional Review Board approval was not needed or sought for our analysis. The NCDB is a hospital-based cancer registry, i.e., jointly maintained by the American College of Surgeons and the American Cancer Society. The database accounts for approximately 70% of the cancer cases in the USA with more than 1,500 accredited programs, and standardizes data elements for patient demographics, tumor characteristics, including stage and site-specific variables, zip code-level socioeconomic factors, facility characteristics, and insurance status. The hospital registries update the vital status (survival) in 5-year increments.

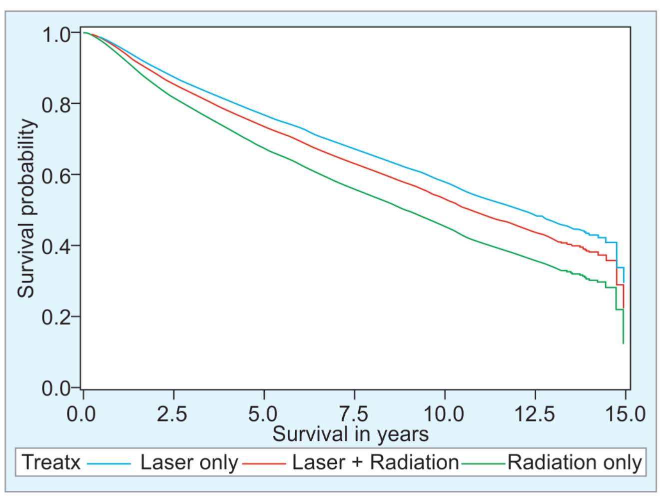
Patients diagnosed with T1 or T2N0M0 laryngeal squamous cell carcinoma antigen (SCCA) from 1998 to 2006 and followed up to end of 2011 who had received either radiation only, laser surgery, or laser surgery and adjuvant radiation were included in the analysis. Exclusion criteria were any patients who received chemotherapy or those with a primary subglottic SCCA. Subglottic cancer was excluded as TLM has not been widely used to treat this subsite of laryngeal SCCA. Descriptive data were gathered and further subdivided by treatment modality for the following characteristics: Sex, age, race, comorbidity score, payer status, income, distance from treating facility, facility type, T-stage, margin status, and primary site. For analysis purposes, age was divided into four subcategories: 18 to 49, 50 to 64, 65 to 74, and 75+. Race was aggregated into white, black, and other. Margin status for patients undergoing TLM was segregated into negative, gross residual tumor, microscopic residual disease not visible to the naked eye, microscopic disease with residual tumor noted, and unknown. Primary site was glottis, supraglottis, or larynx NOS. Facilities were classified based on the NCDB classification into community facilities, comprehensive cancer centers, academic centers, and other. Community facilities treat at least 300 cancer patients annually and have a full range of cancer care services. Comprehensive cancer centers are facilities that offer the same range of services as the community facilities but treat at least 750 patients with cancer annually and conduct weekly cancer conferences. Academic facilities have residency programs and ongoing cancer research.

Statistical Analysis

Chi-square analysis was used to test for differences among the treatment modalities for factors investigated in this study. The 3- and 5-year overall survival (OS) was estimated using the Kaplan–Meier method, and directed adjusted median OS and adjusted survival curves were estimated by using multivariate Cox regression (Graph 1). Log-rank methods were used to determine those factors significant for survival and those significant factors were employed within a multivariable Cox regression model to determine factors independently associated with survival. Statistical analyses were performed with statistical software Statistical Analysis System 9.4 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Data points were collected from 14,276 NCDB patients with early-stage laryngeal cancer who met the inclusion and exclusion criteria. The significant majority (91.2%, $p < 0.0001$) of patients received primary XRT. Only 4.7% (n = 669) of the patients had a laser resection, and 4.0% (n = 570) had laser resection with XRT. Table 1 lists the patient demographics and socioeconomic characteristics by treatment group. The majority of patients were white males, over the age of 50, with no comorbidities, and Medicare or private insurance. Black patients were proportionally less likely to receive primary treatment with TLM than white patients (p = 0.012). Patients with higher comorbidities (score = 2) were more likely to receive laser surgery than those with a score of 0 or



Graph 1: Adjusted median OS by treatment modality

1 (p < 0.001). Less patients in the group treated with primary TLM underwent radiation in the latter half of the study time period 2003 to 2006, compared with the first half 1998 to 2002 (n = 169 *vs* 401 respectively). As income level and distance from the treating facility increased, so did the rates of primary TLM (p = 0.034 and p < 0.001 respectively). While the majority of patients were treated at comprehensive cancer centers (n = 7952), proportionally the highest rates of laser resection were in the academic centers (11.3% *vs* 7.3%).

Table 2 shows the tumor characteristics by treatment modality. Transoral laser microsurgery was utilized mainly for T1/T1a tumors while T2 tumors proportionally underwent primary XRT. Very few patients were diagnosed with T1b tumors. Patients with microscopic residual tumor that was visible surgically underwent adjuvant XRT the majority of the time. The majority of the tumors were glottic (76.8%) and, proportionally, supraglottic tumors were less likely to be treated with primary TLM than glottic (p < 0.0001).

The 3- and 5-year OS for the entire cohort was 79.1 and 68% respectively (Table 3). Glottic SCCA had a 3- and 5-year OS of 82.3 [95% confidence interval (CI) = 81.5–83%] and 71.9% (95% CI = 71.0–772.8%), while supraglottic tumors had a 3- and 5-year OS of 67.8% (95% CI = 66.0–69.6%) and 53.9% (95% CI = 51.9-55.9%) respectively.

Table 1: Descriptive statistics of patient's demographic and socioeconomic status by treatment group

		Radiation only		*Laser only*		*Laser + radiation*		
		n	*%*	*n*	*%*	*n*	*%*	*p-value*
Sex	Male	10697	91.33	552	4.71	463	3.95	0.8366
	Female	2340	91.26	117	4.56	107	4.17	
Age group (years)	18–49	1344	91.87	73	4.99	46	3.14	0.0075
	40–64	5106	92.08	247	4.45	192	3.46	
	65–74	3876	90.99	190	4.44	195	4.58	
	75+	2711	90.13	161	5.32	137	4.55	
Race	White	11419	91.06	602	4.8	519	4.14	0.0121
	Black	1457	93.64	57	3.66	42	2.7	
	Others	161	89.44	10	5.56	9	5	
Charlson	0	4686	92.28	244	4.81	148	2.91	<0.0001
	1	640	92.35	40	5.77	13	1.88	
	2	188	89.1	15	7.11	8	3.79	
	Unknown	7523	90.7	370	4.46	401	4.83	
Payer status	Uninsured	489	94.58	13	2.51	15	2.9	0.0496
	Private	5335	91.51	272	4.67	223	3.83	
	Medicaid	626	92.33	32	4.72	20	2.95	
	Medicare	6151	90.7	337	4.97	294	4.34	
	Unknown	436	92.96	15	3.2	18	3.84	
Year of diagnosis	1998–2002	7523	90.7	370	4.46	401	4.83	<0.0001
	2003–2006	5514	92.18	299	5	169	2.83	
Income	30k	2223	92.16	101	4.19	88	3.65	0.0342
	30–34k	2637	91.85	136	4.74	98	3.41	
	35–45k	3618	91.71	172	4.36	155	3.93	
	46+k	3932	90.14	227	5.2	203	4.65	
Distance	<10 miles	7096	92.64	261	3.41	303	3.96	<0.0001
	10–24 miles	3124	91.45	153	4.48	139	4.07	
	25–49 miles	1529	90.37	95	5.61	68	4.02	
	50–99 miles	578	85	73	10.74	29	4.26	
	100+ miles	223	75.59	61	20.68	11	3.73	
Facility type	Comm CP	1653	93.5	59	3.34	56	3.17	<0.0001
	Comp CP	7374	92.73	237	2.98	341	4.29	
	Acad CP	3452	87.73	340	8.64	143	3.63	
	Other CP	558	89.86	33	5.31	30	4.83	
Facility	Same facility	7596	89.05	500	5.86	434	5.09	<0.0001
	Different facility	5441	94.69	169	2.94	136	2.37	
Delays	0–7	465	35.58	345	26.4	497	38.03	<0.0001
	8–30	7754	97.28	162	2.03	55	0.69	
	31+	4650	97.02	130	2.71	13	0.27	

Table 2: Descriptive statistics of patient's clinical characteristics by treatment group

		Radiation only		Laser only		Laser + radiation		
		n	*%*	*n*	*%*	*n*	*%*	*p-value*
Sex	Male	10697	91.33	552	4.71	463	3.95	0.8366
	Female	2340	91.26	117	4.56	107	4.17	
T-stage	1	4279	90.31	258	5.45	201	4.24	<0.0001
	1A	3498	88.24	282	7.11	184	4.64	
	1B	936	92.13	48	4.72	32	3.15	
	2	4324	94.87	81	1.78	153	3.36	
Clinic path stage	1	8748	89.69	588	6.03	418	4.29	<0.0001
	2	4289	94.85	81	1.79	152	3.36	
Margins	Negative	0	0	425	71.07	173	28.93	<0.0001
	Residual tumor	0	0	16	42.11	22	57.89	
	Micro res tumor eye-	0	0	32	45.71	38	54.29	
	Micro res tumor eye+	0	0	1	3.33	29	96.67	
	Unknown	13037	98.27	91	0.69	139	1.05	
Laser	None laser	13037	100	0	0	0	0	
	Laser only	0	0	669	54	570	46	
Radiation	None radiation	0	0	669	100	0	0	
	Radiation	13037	95.81	0	0	570	4.19	
Chemo	No chemo	13037	91.32	669	4.69	570	3.99	
Primary site	Glottis	9947	90.77	559	5.1	453	4.13	<0.0001
	Larynx, NOS	572	93.46	14	2.29	26	4.25	
	Supraglottis	2518	93.09	96	3.55	91	3.36	

Irrespective of treatment modality, patients with private insurance had a median OS of 13.01 years compared with Medicare (6.45 years), Uninsured (11.14 years), and Medicaid (8.3 years). Median OS for T1 was significantly greater than T2, with 5-year survival of 71.6% for T1 *vs* 56.4% for T2 disease. Glottis primary site had 5-year survival of 71.9% compared with supraglottis with 5-year survival 53.9% ($p < 0.001$). Univariate analysis demonstrated improved median OS for patients treated with either treatment modality at an academic center ($p < 0.0006$). Overall survival for laser *vs* laser + XRT was 10.35 and 10.55 years respectively, compared with 8.68 years for XRT only ($p < 0.001$). Additionally, the univariate analysis revealed a median OS of 9.89 years for glottic lesions *vs* 5.66 years for supraglottic lesions ($p < 0.0001$) (Table 4). Multivariate analysis demonstrates a hazard ratio of 1.55 ($p < 0.0001$) for T2 lesions when compared with T1 (including T1a and T1b) lesions (Table 5). Increased age and decreased income were also associated with poorer OS. Significant disparities were seen with payer source where Medicaid, Medicare, and the uninsured all demonstrated increased hazards ratio (HR) of 1.73 (95% CI = 1.52–1.97), 1.32 (95% CI = 1.22–1.43), and 1.41 (95% CI = 1.20–1.66) respectively, when compared with patients with private insurance ($p < 0.0001$). Supraglottic lesions showed a 1.73 times increased risk of mortality when compared with glottic lesions (95% CI = 1.62–1.86, $p < 0.0001$). When controlling for all significant factors, those patients treated with laser only had a 0.77 HR compared with those treated with primary radiation,

Table 3: Three- and five-year OS by T-stage and treatment and primary site

		Three-year survival			Five-year survival		
		Survival (%)	*Lower (%)*	*Upper (%)*	*Survival (%)*	*Lower (%)*	*Upper (%)*
T-stage	All	79.1	78.4	79.8	68.0	67.2	68.8
	1	82.3	81.1	83.4	71.6	70.2	72.9
	1a	86.0	84.8	87.1	76.8	75.4	78.2
	1b	80.1	77.5	82.7	69.3	66.3	72.3
	2	69.3	67.9	70.7	56.4	54.9	57.9
Treatments	Laser only	87.2	84.5	89.8	78.8	75.5	82.1
	Radiation only	78.5	77.7	79.2	67.2	66.4	68.1
	Laser + radiation	81.7	78.5	85.0	72.6	68.8	76.5
Primary site	Glottis	82.3	81.5	83.0	71.9	71.0	72.8
	Larynx	70.6	66.8	74.3	60.0	55.8	64.1
	Supraglottis	67.8	66.0	69.6	53.9	51.9	55.9

Table 4: Univariate analysis of survival by demographics (age, race, facility type, sex, insurance status, income, education), tumor characteristics (stage – T1, T1a, T1b, T2, and grade), margin status, and treatment type

	Subjects	*n*	*MOS*	*Lower*	*Upper*	*Log-rank*	*Trend*
Sex	Male	11724	8.99	8.74	9.28		
	Female	2568	8.54	7.92	9.01		
AJCC stage	Stage I	9750	10.2	9.89	10.42		
	Stage II	4526	6.2	5.90	6.49		
Age (years)	18–49	1463	>14.48			<0.001	<0.001
	50–64	5554	12.35	11.83	12.98		
	65–74	4263	8.35	7.95	8.65		
	75+	3012	4.76	4.50	4.96		
Race	White	12555	8.91	8.68	9.22	0.0021	
	Black	1557	8.41	7.64	9.25		
	Other	180	11.93	9.54			
Comorbidity	0	5083	8.84	8.57	9.24	<0.001	
	1	695	6.98	6.14	7.76		
	2	211	2.85	2.47	3.68		
	Unknown	8303	9.03	8.74	9.37		
Payer	Uninsured	520	11.14	8.76		<0.001	
	Private	5835	13.01	12.53			
	Medicaid	679	8.3	7.16	9.23		
	Medicare	6789	6.45	6.26	6.67		
	Unknown	469	9.35	7.96	10.87		
Income	<30k	2416	7.84	7.42	8.45	<0.001	<0.001
	30–34k	2873	8.5	7.95	8.85		
	35–45k	3947	8.59	8.24	9.03		
	46+k	4370	9.95	9.56	10.42		
Facility type	Comm CP	1769	8.42	7.75	8.99	0.0006	
	Comp CP	7961	8.68	8.46	8.97		
	Acad CP	3940	9.61	9.26	9.96		
	Other	622	8	7.05	10.55		
Delays in tx	0–7	1309	9.86	9.227	10.55	<0.001	<0.001
	8–30	7981	9.24	8.841	9.512		
	31+	4796	8.19	7.748	8.605		
Treatment	Radiation	13047	8.68	8.48	8.91	<0.001	<0.001
	Laser only	671	10.35	9.90	12.84		
	Laser + radiation	574	10.55	9.40	13.40		
T-stage	1	4740	9.51	9.11	9.89	<0.001	<0.001
	1A	3967	11.53	10.85	12.16		
	1B	1016	9.07	8.49	9.89		
	2	4569	6.23	5.91	6.50		
Clin path stage	1	9759	10.19	9.89	10.42	<0.001	
	2	4533	6.23	5.91	6.50		
Laser	No laser	13047	8.68	8.482	8.906	<0.001	
	Laser	1245	10.55	9.9	12.46		
Radiation	No radiation	671	10.35	9.9	12.84	<0.001	
	Radiation	13621	8.76	8.539	8.986		
Margins	Negative	600	12.84	10.11		<0.001	
	Residual	39	13.75	4.791			
	Micro res eye-	71	9.64	6.563	12.22		
	Micro res rye+	30	>12.8	4.991			
	Unknown	13279	8.71	8.515	8.944		
Primary site	Glottis	10969	9.89	9.61	10.19	0.0001	
	Larynx	613	6.92	5.938	7.608		
	Supraglottis	2710	5.66	5.27	6.075		

Table 5: Multivariate Cox regression

		HR	*Lower*	*Upper*	*p-value*
Sex	Female	1.00			
	Male	1.14	1.07	1.49	0.0001
Race	White	1.00			
	Black	1.01	0.92	1.10	0.883
	Others	0.64	0.49	0.84	0.001
Age (years)	18–44	1.00			
	45–64	1.54	1.35	1.74	<0.0001
	65–74	2.30	2.00	2.63	<0.0001
	75+	4.54	3.95	5.22	<0.0001
Payer	Private	1.00			
	Medicaid	1.73	1.52	1.97	<0.0001
	Medicare	1.32	1.22	1.43	<0.0001
	Uninsured	1.41	1.20	1.66	<0.0001
	Unknown	1.19	1.02	1.39	0.030
Income	45+k	1.00			
	30 k	1.21	1.11	1.31	<0.0001
	30–34k	1.14	1.05	1.23	0.001
	35–45k	1.09	1.01	1.16	0.019
Charlson	0	1.00			
	1	1.14	1.01	1.30	0.036
	2	2.17	1.82	2.59	<0.0001
	Unknown	1.06	0.99	1.12	0.085
Distance	<10 miles	1.00			
	10–24 miles	0.99	0.93	1.06	0.792
	25–49 miles	1.00	0.92	1.09	0.999
	50–99 miles	0.89	0.78	1.02	0.093
	100+ miles	1.09	0.90	1.32	0.384
Diag txt facility	Same facility	1.00			
	Different facility	0.99	0.93	1.04	0.591
Facility	Academic CP	1.00			
	Comm CP	1.09	0.99	1.19	0.071
	Comp CP	1.06	0.99	1.12	0.096
	Other CP	1.15	0.94	1.41	0.171
Delays treat (days)	31+	1.00			
	0–7	1.10	0.96	1.25	0.163
	8–30	0.87	0.82	0.92	<0.0001
T-stage	1	1.00			
	1A	0.93	0.86	1.00	0.044
	1B	1.18	1.05	1.31	0.005
	2	1.55	1.46	1.66	<0.0001
Margins	Negative	1.00			
	Micro res tumor eye+	1.61	0.82	3.06	0.169
	Micro res tumor eye-	1.52	1.01	2.36	0.043
	Residual tumor	1.17	0.64	2.01	0.661
	Unknown	1.23	0.91	1.58	0.192
Primary site	Glottis	1.00			
	Larynx, NOS	1.33	1.18	1.51	<0.0001
	Supraglottis	1.73	1.62	1.86	<0.0001
Treatment	Radiation only	1.00			
	Laser only	0.77	0.57	1.01	0.055
	Laser + radiation	0.65	0.50	0.84	0.001

although this did not achieve statistical significance at the p ± 0.05 level (95% CI = 0.57–1.01, p = 0.055). The patients who were treated with laser resection followed by adjuvant radiation demonstrated a reduction in mortality (HR = 0.65, 95% CI = 0.5–0.84, p = 0.001) when compared with radiation alone.

DISCUSSION

Overall, our results showed an improved OS for patients treated with laser surgery ± adjuvant therapy when compared with primary RT. However, when controlling for all significant factors, those patients who were treated with laser surgery alone did not achieve a statistically significant reduction in mortality when compared with those treated with radiation alone. These results highlight the conflicting evidence, i.e., available regarding primary treatment for laryngeal cancer.

With comparable survival outcomes between treatment modalities, there is increasing importance of understanding other patient and tumor characteristics that affect outcomes. Chen et al[21] examined survival outcomes in patients with laryngeal cancer that were treated at high-volume *vs* low-volume treatment facilities. This study demonstrated that in 11,110 patients, those treated at high-volume facilities had improved survival over those treated at low-volume facilities. Additionally, these authors observed that in this large patient group, those undergoing surgical treatment for early-stage laryngeal cancer had significantly better 5-year survival rate at 68% compared with 59% in those undergoing primary RT.[21] This is one of the few large-scale studies to report a survival advantage for those patients undergoing surgical resection for T1-2 laryngeal squamous cell carcinoma. In contrast, a single-center case series reported by Comert et al[17] who showed equivocal 3- and 5-year DFS in 140 patients with T1 and T2 laryngeal cancer that were treated with either transoral endolaryngeal microscopic diode laser surgery *vs* XRT.

While Chen et al included both open and endoscopic techniques in their evaluation, our study only included TLM and excluded any other open partial surgical therapies. Though using the same database, Chen et al only included patients that were diagnosed from 1996 to 1998, while our study included patients diagnosed from 1998 to 2006. Both studies highlight a discrepancy in survival based on treatment facility, insurance status, and race. Our multivariate analysis concurs that patients with Medicare, Medicaid, or uninsured had worse outcomes when compared with privately insured. In addition, our multivariate analysis reflects that age >44 years, Charlson score >1, T2 stage of primary tumor, and supraglottic subsite are also significantly associated with worse outcomes.

Another recent study by Misono et al[22] looked at patients with T1 glottic lesions and concluded that those patients whose treatment included surgical therapy had better survival than those treated with XRT only.[22] This study utilized the Surveillance, Epidemiology, and End Results (SEER) Medicare database, which only includes patients with Medicare Part A and B, and only patients >66 years. In this patient group, these authors found that patients undergoing surgical excision or surgery plus XRT exhibited better OS compared with patients who were treated nonsurgically. They were also able to identify black race and increased medical comorbidity with worse survival. Despite this study being limited by only including Medicare-enrolled patients older than 66 years, and those with T1 lesions only, they were still able to demonstrate black race and increased comorbidity index as being negatively associated with survival.

In our study, the survival advantage for surgery over XRT did not reach statistical significance; however, the data imply a trend toward improved survival. The TLM plus XRT group did reach significance, as would be expected when comparing single modality *vs* multimodality therapy, with the suspicion that surgical examination better identified those deeply invasive tumors or paraglottic space invasion that was not easily identifiable on preoperative workup. To fully elucidate differences in outcomes for primary TLM *vs* XRT, a prospective, randomized controlled trial would likely be required with extensive follow-up. While this may be prohibitive from a cost perspective, if we assume a multivariate HR of 0.77 for TLM compared with XRT, a two-tailed study powered to 0.8 with a significance value set at p = 0.05 would only require 185 patients in each treatment arm to adequately power the study (Stata Corp.). Given the advent of recent multiinstitutional, oropharyngeal surgical trials, these numbers do not seem so daunting.

There were many limitations to the present study. The NCDB does not maintain data on recurrence and smoking status, both of which are significant factors for survival in head and neck cancer patients. Due to the retrospective nature of the study, selection bias, especially for chosen treatment modality, is an issue. Within the TLM group, patients were more likely to receive laser surgery upfront if they had a T1 glottic tumor, rather than a supraglottic or T2 SCCA. Additionally, laser surgery was administered more often at academic centers. These factors may explain the lack of significance seen with the HR in the multivariate analysis when comparing the laser only cohort to the radiation only patients (p = 0.055). Many other subtle issues can determine choice of treatment, such as the functional status of the voice, surgeon comfort, availability of technology, etc. The NCDB also does not collect data on cause of death, which makes OS the reported marker for mortality. Thus, patients who were more debilitated or more likely to die of nonlaryngeal cancer-related causes may have received primary radiation, which could account for the survival differences.

CONCLUSION AND CLINICAL SIGNIFICANCE

Early-stage laryngeal cancer is amenable to XRT and/or surgical resection as primary therapy. Our study concludes that patients with early-stage laryngeal cancer showed improved survival when treated with TLM *vs* XRT; however, these results did not reach significance when controlling for other factors. However, those patients treated with laser therapy and radiation did achieve a statistically significant improved survival over radiation alone, suggesting that surgical staging may play an important role in this disease process. Advanced age, increased comorbidity index score, lower income, black race, Medicare, Medicaid, and uninsured, T2 stage, and supraglottic subsite were all associated with worse OS.

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