


# Treatment Patterns in Veterans with Laryngeal and Oropharyngeal Cancer and Impact on Survival

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**Objectives:** Veterans with laryngeal and oropharyngeal cancer remain an understudied patient population despite a high incidence of disease and decreased survival compared to the general population. Our objective was to evaluate treatment patterns for laryngeal and oropharyngeal cancer in patients treated at one of the Veterans Health Administration's busiest cancer centers in order to generate some basic benchmarks for treatment delivery in the veteran population.

**Methods:** We reviewed 338 patients treated at the Michael E. DeBakey Veterans Affairs Medical Center between 2000 and 2012.

**Results:** Oropharyngeal site and advanced age were associated with worse overall and disease-free survival. Treatment periods (mean) were as follows: 1) referral-diagnosis, 26 days; 2) diagnosis-surgery, 29 days; and 3) diagnosis-radiation, 58 days. Adjuvant radiation was initiated within 6 weeks of surgery in 42% of patients and 68% of patients had a total treatment package time  $\leq 100$  days. Time from diagnosis to treatment initiation, surgery to adjuvant radiation interval and total treatment package time did not impact survival.

**Conclusions:** This study establishes basic benchmarks for laryngeal and oropharyngeal cancer treatment delivery in veterans. Additional efforts are warranted to improve consistency and provide treatment in line with NCCN recommendations and literature consensus.

**Key Words:** Veteran, oropharyngeal cancer, laryngeal cancer, radiation, treatment package.

**Level of Evidence:** 2b

## INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) is an aggressive malignancy which remains poorly studied compared to more common diseases such as lung, breast, and prostate cancer.<sup>1</sup> The incidence of HNSCC in

certain subsites such as the oropharynx is increasing at a nearly epidemic rate.<sup>2,3</sup> Unfortunately, appropriate treatment delivery for HNSCC remains a challenge.<sup>4-6</sup> Tertiary institutions often tailor National Comprehensive Cancer Network (NCCN) guidelines to their specific patient populations through internal algorithms in order to better serve that patient population.<sup>7,8</sup> This is particularly important in light of significant racial/ethnic and socioeconomic disparities in HNSCC treatment selection and clinical outcomes.<sup>8-11</sup>

HNSCC care within the Veterans Health Administration (VHA) poses additional challenges. Veterans often present with variable socioeconomic status, increased age and comorbidity burden and a substantially higher exposure to traditional carcinogens, which modifies not only their baseline HNSCC development risk, but often contributes to advanced disease stage at presentation.<sup>12-14</sup> In the United States, the VHA provides a vertically and horizontally integrated health system which can allow us to understand deficiencies in HNSCC treatment delivery and test potential means of improving access to multi-modality care and care delivery. However, baseline descriptive studies of HNSCC incidence/prevalence, oncologic outcomes and treatment delivery in the modern era within the VHA are lacking.<sup>15-17</sup>

We recently published oncologic outcomes for patients with laryngeal and oropharyngeal squamous cell carcinoma (SCC) treated at one of the largest VHA cancer centers in the country.<sup>12-14</sup> Our results demonstrate that outcomes

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for veterans with laryngeal and oropharyngeal SCC are comparable to published series from other tertiary centers and prospective clinical trials.<sup>12-14</sup> Here we sought to evaluate treatment patterns associated with multi-disciplinary treatment delivery for laryngeal and oropharyngeal cancer. We focused on these two disease sites because their incidence in the veteran population continues to be high and because they are disproportionately treated with radiation which in our experience can generate challenges in treatment initiation and timely completion. Our primary goal was to evaluate the time frames associated with diagnosis as well as treatment initiation and completion and identify potential opportunities for improvement in treatment delivery. To our knowledge this is the largest veteran cohort to undergo this analysis in the modern era.

## METHODS

Following approval by the Baylor College of Medicine and the MEDVAMC institutional review boards, we reviewed the records of all patients with previously untreated oropharyngeal and laryngeal SCC treated at the MEDVAMC between January 1, 2000 and April 1, 2012. Waiver of consent was granted by the institutional review board for the current study. Exclusion criteria included previous treatment of disease, recurrent disease, or palliative treatment selection. Demographic information was recorded, including age, gender, marital status, race, smoking history, and alcohol consumption. Clinical pathologic features were collected including clinical stage according to the American Joint Commission on Cancer (Edition 7) staging system and tumor grade of initial biopsy specimens. Results of diagnostic procedures, including imaging results, biopsies and fine-needle aspirations, were recorded as well as the treatments rendered and the associated dates.

A multidisciplinary head and neck tumor board consisting of head and neck surgeons, medical oncologists, and radiation oncologists determines the treatment plan for all head and neck cancer patients. Patients are scheduled for regular follow-up for the first 5 years post-treatment completion and are encouraged to continue yearly follow-up thereafter in the absence of new concerning symptoms. For the purpose of the current analysis, patients which were slated for palliative treatment or stopped treatment prematurely were excluded since their data would significantly affect the measured time intervals described below. From our larynx cohort we excluded 11 patients, which did not receive treatment with curative intent and 3 patients who refused or were unable to complete adjuvant radiation. From our oropharynx cohort we excluded 15 patients, which were treated with palliative intent based on disease stage and an additional 24 patients which refused treatment. As a result, the current study evaluates 86% of the patients which presented with a new laryngeal or oropharyngeal cancer during this time period.

It is well established by our group and others that incomplete treatment for HNSCC is associated with poor oncologic outcomes.<sup>12</sup> Patients who experienced treatment breaks or missed radiation sessions were included in the analysis, since this is an unwanted but realistic feature of HNSCC treatment in the non-clinical trial setting.<sup>12</sup> For the purposes of our analysis, treatment package time was defined as the time interval from the date of surgery to the end of the adjuvant radiation treatment; this is consistent with previous literature.<sup>18</sup> For the purposes of analysis, all treatments refer to curative intent treatments. Specifically, the term "surgery" refers to ablative, curative intent primary treatment. Radiation refers to curative intent (not palliative) radiation. The treatment package time

TABLE I.  
Patient Characteristics.

		Patients (n = 338)	
		Median	Range
Age (yr)		61	41-88
Income (\$)		\$49,407	\$21,483-\$112,218
Distance from MEDVAMC (miles)		25.4	2.1-449.3
		N	%
Gender	male	335	99
	female	3	1
Race	white	245	73
	black	93	27
Risk factors	tobacco	312	92
	alcohol	274	81

analysis was restricted to the subset of patients which had curative intent primary surgery followed by adjuvant radiation. Introduction of intensity modulated radiotherapy (2006-2007) was also incorporated as a time point in the analysis.

Distance calculations were performed using CDXZip-Stream 10.2.1.25 (Hughes Financial Services Inc., Herndon, VA, USA). Income data was extracted from the University of Michigan Population Studies Center, Institute for Social Research using median and mean household income data for 2006-2010 (<https://www.psc.isr.umich.edu/dis/census/Features/tract2zip/index.html>). Statistical analysis was performed using SAS 9.4 (SAS/STAT 14.1) (SAS Institute, Cary, NC, USA). The effect of patient and tumor characteristics, and treatment on overall and disease-free survival was ascertained using Kaplan-Meier curves and log-rank estimates of statistical significance as well as using Cox regression analysis.

## RESULTS

### Patient and Tumor Characteristics

A total of 338 patients were identified using the inclusion and exclusion criteria detailed above (Table I) with a median follow-up of 2.5 years (mean = 3.5 years). Nearly all patients had a history of tobacco (92%) (mean = 55 pack years, median = 50 pack years) and alcohol consumption (81%). A majority of patients lived within 100 miles from the MEDVAMC; median incomes for individual patient zip codes ranged from \$21,483 to \$112,218 (Supplementary Fig. 1).

Tumors were nearly evenly divided between laryngeal and oropharyngeal sites (Table II). Nearly half of all tumors were staged T3-4 and 46% of tumors were N0. Laryngeal tumors more frequently presented as early T stage (T1-2) compared to oropharyngeal tumors. T4 tumors were equally represented in both cohorts but oropharyngeal tumors were associated with a nearly 3-fold increase in the frequency of N2 stage (Table II). Overall and disease-free survival was significantly higher for patients with laryngeal cancer compared to oropharyngeal cancer (Fig. 1). For patients with laryngeal tumors, N stage impacted disease-free survival whereas for patients with oropharyngeal tumors, T stage

TABLE II.  
Tumor Characteristics.

		Number (n = 338)	%	Larynx (n = 187)	%	Oropharynx (n = 151)	%	P value*
<b>T stage</b>	1	81	23	59	32	22	15	.0003
	2	106	32	58	31	48	32	NS
	3	72	21	32	17	40	27	.0262
	4	79	24	38	20	41	27	NS
<b>N stage</b>	0	159	46	127	68	31	21	.0001
	1	27	9	14	8	13	9	NS
	2	139	41	43	23	96	64	.0001
	3	14	4	3	2	11	7	.0234

\*P values calculated using the N-1 chi-squared test

impacted overall survival (Supplementary Fig. 2). The impact of HPV/p16 status on oropharyngeal cancer outcomes was previously published by our group in the entire cohort of OPSCC patients for this time period.<sup>12</sup> For those patients with OPSCC, treated with curative intent, included in this analysis for which p16 data was

available (n = 131), 49 patients were p16 negative (-) and 82 patients were p16 positive (+). Both disease-free and overall survival were significantly lower in p16- patients as expected (Supplementary Fig. 3). The lower survival of p16- OPSCC patients of the oropharyngeal cohort decreased survival for the entire OPSCC cohort.

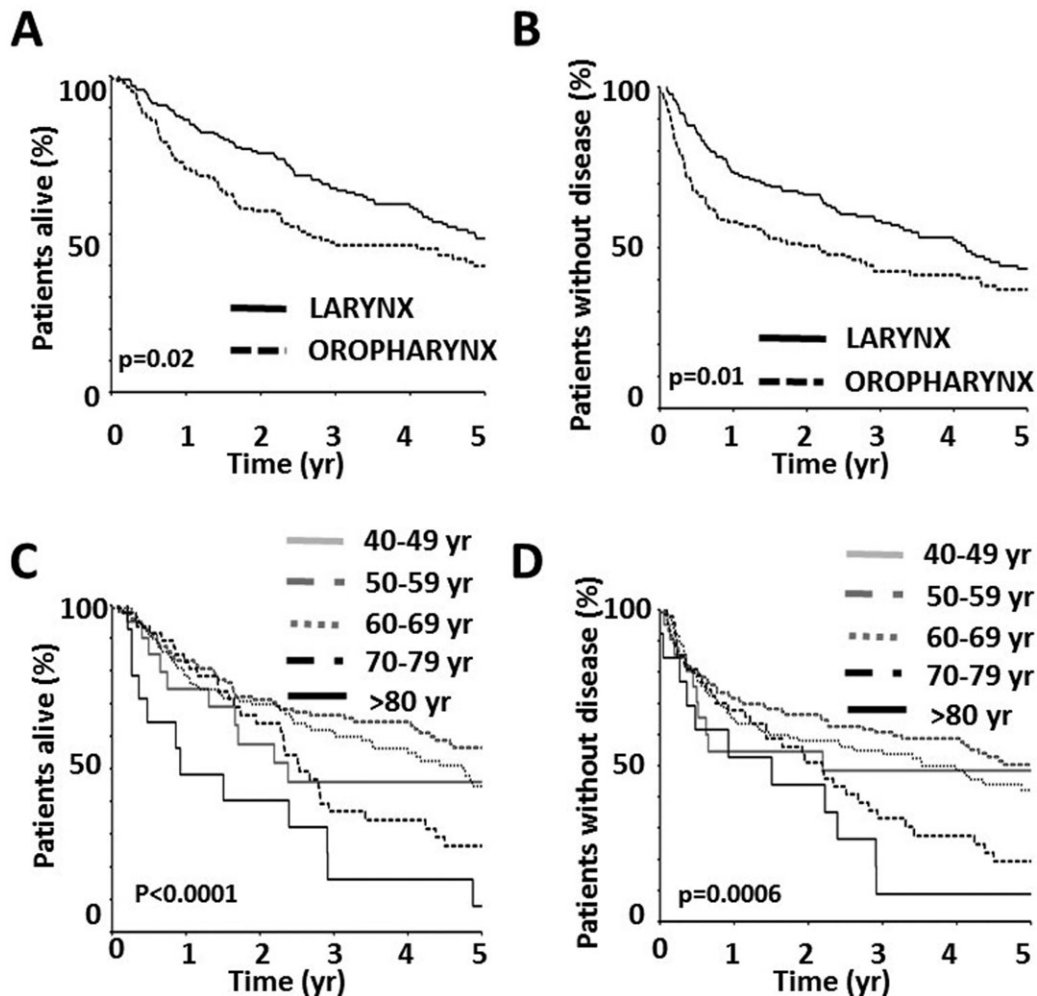


Fig. 1. Impact of site and age on survival. Patients with oropharyngeal SCC demonstrated decreased overall (A) and disease-free (B) survival compared to patients with patients with laryngeal SCC. Advanced age had an impact on both overall (C) and disease-free survival (D). SCC = squamous cell carcinoma p-values calculated using log-rank test.

TABLE III.  
Treatment Characteristics.

Treatment	Number (n = 338)	%	Larynx (n = 187)	%	Oropharynx (n = 151)	%	P value*
Primary surgery	21	6	16	9	5	3	.0244
Primary radiation (with or without chemotherapy)	263	78	122	65	140	93	.0001
Surgery + radiation (with or without chemotherapy)	55	16	49	26	6	4	.0001

\*P values calculated using the N-1 chi-squared test

Advanced age was associated with decreased overall and disease-free survival, driven primarily by the octogenarian cohort (Fig. 1).

### Treatment Characteristics

Our previous publications detail compliance with NCCN guidelines as it relates to treatment selection.<sup>12,13</sup> A majority of patients underwent external beam radiotherapy (EBRT) in the primary or adjuvant setting (Table III). Due to the higher frequency of T1 laryngeal tumors, a higher percentage of patients with laryngeal disease underwent surgical treatment without adjuvant radiation compared to patients with oropharyngeal disease. The majority of patients which had surgery followed by adjuvant radiation were patients with laryngeal tumors, consistent with current treatment guidelines for T4 laryngeal disease (Table III).

### Pretreatment Evaluation

At our institution, the primary referral pattern is through the MEDVAMC Otolaryngology-Head and Neck Surgery (Oto-HNS) Clinic. The most common referring service (70%) was the primary care (PrimeCare) service line within the MEDVAMC and outlying PrimeCare clinics. The second most common referring service was the Emergency Room/Urgent Care (17%) service line. Mean time from referral to diagnosis was 26 days. Surgical treatment was initiated within 30 days of tissue diagnosis but initiation of radiation based primary treatment required approximately twice as long (Table IVA). Time from referral to surgical intervention was 75 days when surgery alone was required and 53 days when adjuvant treatment was required following ablative surgery. Among patients which had an interval >100 days prior to surgical intervention (n = 10), 4 delays were due to comorbid conditions, 3 due to patient related delays in scheduling, and 3 due to potential system failure to schedule surgery in a shorter time period. Time from referral to primary radiation start was 89 days when radiation alone was required and 72 days when chemotherapy was required along with radiation (Table IVB, Table V). Among patients which had an interval >100 days prior to radiation treatment from referral (n = 50), 14 delays were due to comorbid conditions, 7 due to patient related delays in scheduling, and 6 due to system related issues including transfer of care from an outside institution or failure to schedule the patient sooner; specific reasons could not be identified for the remaining patients. Neither time from referral to radiation start, nor time from

diagnosis to radiation initiation were significantly changed when dichotomized to pre-2006 and post-2006 time periods (P values .59 and .34, respectively). Mean time from referral to radiation oncology to first radiation oncology visit was 16 days (median = 13 days). Mean time from referral to first radiation fraction was 49 days (median = 42 days).

Patients with advanced disease demonstrated shorter times to tissue diagnosis and treatment initiation. As shown in Table IV, patients which required multi-modality treatment (surgery followed by adjuvant treatment or chemo-radiation) experienced shorter intervals between referral and treatment initiation (P = .007 for radiation vs. chemo-radiation, P < .001 for surgery followed by adjuvant treatment vs. radiation-based treatment). Of 200 patients referred by the PrimeCare service line, 62% presented with T1-2 disease, while 38% presented with T3-4 disease. In contrast, among 45 patients referred by the Emergency Room/Urgent Care service line, 24% presented with T1-2 disease, while 76% presented with T3-4 disease. This difference is highly statistically significant (P < .0001). Disease stage and site were partially reflected in the reason

TABLE IV.  
Pretreatment Patterns.

A			
Pretreatment parameters	Mean (days)	Median (days)	
Referral—ENT visit	26.0	16.5	
Referral—diagnosis	25.8	18	
Diagnosis—surgical treatment (primary)	28.8	24	
Diagnosis—radiation treatment (primary)	57.6	48	
Diagnosis—radiation treatment (adjuvant)	78.1	71	
B			
Pretreatment parameters	Mean (days)	Median (days)	Range (days)
Referral—surgery (surgery only tx)	75	70	1–226
Referral—surgery (surgery + adjuvant tx)	53	40	7–179
Referral—radiation (primary radiation only)	89	81	17–212
Referral—radiation (primary chemo-radiation)	72	70	18–258



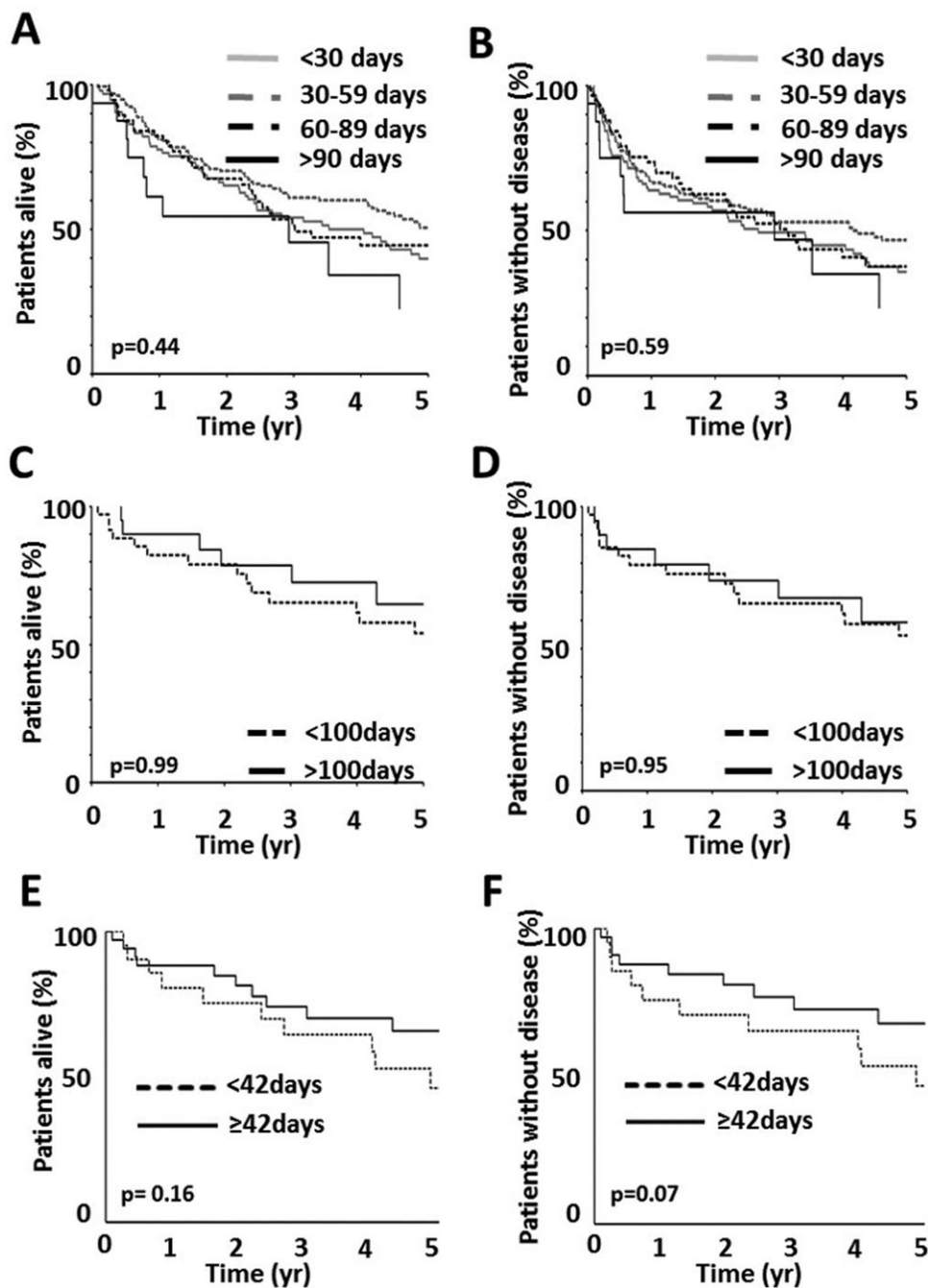


Fig. 2. Impact of interval to treatment and treatment package time on survival. Time interval between diagnosis and treatment was not significantly associated with overall survival (A) or disease-free survival (B). Total treatment package time for patients treated with surgery followed by adjuvant radiation +/- chemotherapy was not associated with overall (C) or disease-free survival (D). Delay of adjuvant radiation following surgery past 42 days did not impact overall (E) or disease-free survival (F) p-values calculated using log-rank test.

for consultation. Of note, only 20 patients were referred for a diagnosis of “cancer” or “carcinoma.” The remaining consults could be grouped into 3 categories: symptom based (dysphagia, dysphonia, odynophagia), exam finding based (neck mass, upper-aerodigestive tract mass or ulcer), or airway concern based (shortness of breath, stridor, hemoptysis). Patients with laryngeal tumors were primarily referred for a symptom (dysphagia, dysphonia, odynophagia) irrespective of T stage (T1 = 95%, T2 = 89%, T3 = 80%, T4 = 77%). Patients with oropharyngeal tumors were primary referred for an exam finding (mass) irrespective of T stage (T1 = 90%, T2 = 82%, T3 = 54%, T4 = 84%).

Overall, patients with  $T \leq 2$  had a mean of 22 days from referral to first evaluation and 34 days from referral to tissue diagnosis compared to  $T \geq 2$  tumors for which the same time periods were 16 ( $P = .04$ ) and 12 days respectively ( $P = .01$ ). For T4 tumors, time from referral to first evaluation was truncated to 11 days and time from referral to tissue diagnosis to 3 days. For patients treated definitively with radiation, the time from diagnosis to EBRT initiation did not differ substantially based on T stage ( $T \leq 2$  vs.  $T \geq 2$ ;  $P = .8$ ; T4 interval mean = 54 days). For patients treated surgically, mean interval from diagnosis to surgery for  $T \leq 2$  was 38 days compared to 24 days for  $T \geq 2$  ( $P = .03$ ) and 23 days for T4 tumors.

TABLE V.  
Treatment Patterns.

Treatment parameters	Mean (days)	Median (days)
Treatment time—radiation (primary)	52.7	51
Treatment time—radiation (adjuvant)	52.4	49
Surgery → radiation interval	51.2	44
Treatment package time (surgery + radiation)	103.6	94

Time from diagnosis to treatment did not impact overall or disease free survival, but time from referral to treatment impacted both overall and disease-free survival (Fig. 2, Supplementary Fig. 4). Importantly, those patients with a short interval from referral to treatment had worse survival than those with a longer interval, consistent with the data summarized above for more advanced tumors (Table VI).

### Treatment Patterns

Most patients underwent radiation based treatment, consistent with national trends (Table III).<sup>2,3,5,12,13,19–21</sup> Chemotherapy was added to radiation in the definitive setting in 152 of 262 patients and in the adjuvant setting in 13 of 55 patients. Patients generally completed their course of radiation with a mean and median duration consistent with routine clinical practice (Table V). For those patients who underwent primary surgery followed by adjuvant radiation, the mean and median interval between surgery and adjuvant EBRT initiation was greater than the NCCN recommended interval ( $\leq 6$  weeks). Forty-two percent of patients had a treatment interval treatment package time  $\leq 6$  weeks.

Previous publications have generated a treatment package time benchmark of 100 days.<sup>22</sup> Our median treatment package time was 94 days; 68% of patients had a treatment package time  $\leq 100$  days. The addition of chemotherapy did not significantly impact treatment package time ( $P = .821$ ). Among patients with treatment package times  $>100$  days for which a potential reason could be identified, 3 treatment delays occurred due to patients repeatedly postponing appointments, 2 apparent delays in evaluation, and 5 delays secondary to prolonged hospitalization, concurrent malignancies/secondary illnesses; 2 delays were related to postoperative non-healing wounds. Treatment package time did not differ when dichotomized based on diagnosis pre-2006 and post-2006 ( $P = .260$ ). The retrospective nature of the data collection and the granularity of the data available did not allow us to determine whether need for dental extractions played a role in treatment delay.

### Treatment Pattern Impact on Clinical Outcomes

Neither surgery-adjuvant EBRT interval nor total treatment package time significantly impacted clinical outcomes (Fig. 2, Supplementary Table 1). Advanced T stage and advanced age significantly impacted DFS and

OS. The impact of age was primarily driven by survival in in the octogenarian cohort and advancing age did not generate a continuous decrease in survival (Table VI).

## DISCUSSION

Despite advances in targeted agents, EBRT techniques and immunotherapy, oncologic outcomes for patients with advanced stage HNSCC remain poor with the unique exception of HPV-driven malignancies.<sup>2,3,5,23–25</sup> Improving cancer care delivery is critical to improving clinical outcomes. Identifying effective means of cancer care delivery improvement, however, has proved challenging. Although current NCCN guidelines support the use of adjuvant EBRT within 6 weeks of surgery, and studies from multiple institutions support the value of treatment package times shorter than 100 days, literature on additional treatment parameter development is lacking.<sup>22,26–28</sup>

TABLE VI.  
Multivariate Analysis of Overall and Disease-Free Survival.

A						
Overall survival						
Variable	Reference	P value	HR	95% CI		
<b>Site</b>	larynx	oropharynx	.2532	0.761	0.477	1.216
<b>T stage</b>	2	1	.0575	1.672	0.984	2.843
	3		.0187	1.995	1.122	3.549
	4		.0012	2.737	1.488	5.036
<b>N stage</b>	1	0	.9306	1.032	0.506	2.106
	2		.6636	0.899	0.555	1.455
	3		.3877	1.496	0.6	3.735
<b>Age</b>	50–59	40–49	.7671	0.895	0.429	1.867
	60–69		.7343	1.138	0.54	2.394
	70–79		.1248	1.843	0.844	4.023
	$>80$		.0041	4.062	1.558	10.587
<b>Distance</b>	$>50$ miles	$<50$ miles	.5297	1.141	0.757	1.719
<b>Median income</b>	$>50,000$	$<50,000$	.4064	1.182	0.796	1.756
B						
Disease free survival						
Variable	Reference	P value	HR	95% CI		
<b>Site</b>	larynx	oropharynx	.0935	0.667	0.415	1.071
<b>T stage</b>	2	1	.0713	1.627	0.959	2.76
	3		.007	2.214	1.242	3.946
	4		$<.0001$	3.479	1.901	6.369
<b>N stage</b>	1	0	.9939	1.003	0.484	2.076
	2		.2003	0.729	0.45	1.182
	3		.8693	0.929	0.388	2.226
<b>Age</b>	50–59	40–49	.5885	0.817	0.393	1.7
	60–69		.7694	1.119	0.529	2.367
	70–79		.1566	1.755	0.806	3.823
	$>80$		.0044	3.993	1.54	10.356
<b>Distance</b>	$>50$ miles	$<50$ miles	.6447	1.104	0.725	1.683
<b>Median income</b>	$>50,000$	$<50,000$	.4316	1.174	0.787	1.752

CI = confidence interval; HR = hazard ratio.

The US Veterans Affairs medical system provides a vertically and horizontally integrated medical system that services a large, diverse patient population across the entire geographical landscape of the United States. As such, it provides a unique opportunity to study, and potentially improve, care delivery patterns for patients with HNSCC, particularly in an understudied patient population.<sup>12,13,29</sup> To our knowledge, this is the largest single institution veteran cohort to undergo this type of analysis in the modern era. We have previously shown comparable outcomes with published series for patients with laryngeal and oropharyngeal SCC. Two basic questions remain: 1) Can we do better?; and 2) How do we do better?

The relationship between pretreatment parameters and surveillance metrics and survival remains unclear.<sup>27</sup> Our own data indicate that pretreatment parameters present a particularly difficult problem in the context of potential benchmarking. It is important to note the disparity between mean and median times from referral to first evaluation in our dataset; this is primarily due to essentially a bimodal clustering of patients. A majority of patients with advanced T3/T4 tumors presented through the MEDVAMC ER/UC service line and were often evaluated clinically within 24 hours of initial presentation to the institution. Since many of these patients presented either with airway compromise or failure to thrive, their evaluation was greatly expedited, in large part due to the availability of Oto-HNS within the same facility. Patients with advanced stage disease therefore will likely undergo a truncated pretreatment work-up and faster treatment initiation, but they will also generally present with worse rates of disease control and overall survival. In contrast, patients with early/intermediate stage disease are generally referred for initial Oto-HNS evaluation on the basis of symptoms which can be vague and generally non-specific to HNSCC. Absent resources to evaluate every referral for “dysphagia” or “hoarseness” within a 48- to 72-hr time period, institutional resources and efforts must be dedicated to development of streamlined referral and diagnostic pathways for patients with laryngeal and oropharyngeal cancers. In an integrated medical system, we believe this presents an important unmet need and opportunity for cooperative group prospective investigation. The impact of the current electronic medical record on treatment initiation and delivery remains unclear at this time. Its integrated nature allows treatment teams to have rapid access to all patient related data and provider notes not only within a given institution, but also across VHA institutions. However, it lacks some of the built-in applications common to commercial programs which might trigger automatically to identify potential diagnostic and treatment delays.

Within an integrated system, the treatment team can adapt to advanced stage disease, as demonstrated by a truncated diagnostic period and faster initiation of surgical treatment for patients with advanced T stage disease, particularly T4 disease. However, the increased interval between surgery and adjuvant EBRT described in our patients may reflect the extensive work-up and preparation required to initiate HNSCC EBRT despite

the ability to operate at earlier time points. Therefore, the impact of pretreatment parameters (ie, referral diagnosis, pre-referral work-up, patient compliance with referral) is highly unlikely to be fully understood using any means other than prospective, granular data collection within large academic institutions and integrated HNSCC treatment delivery systems. The impact of treatment package time on oncologic outcomes has been described by multiple authors.<sup>19,22,28</sup> However, treatment delays continue to occur frequently at a national level.<sup>26</sup> In our patients, neither treatment package time nor interval between surgery and adjuvant radiation had a significant impact on survival. We do not think this is because these parameters are not important to survival; conversely, we have undertaken prospective efforts to improve compliance with these metrics. We believe that in this patient population the survival impact of these parameters is potentially overwhelmed by other clinical-pathologic parameters.

Since this is a retrospective study, we cannot provide granular insight into patient versus institutional factors associated with treatment patterns for every individual patient. In order to increase the granularity and quality of future data collection we have instituted a prospective data collection effort for new HNSCC patients evaluated at the MEDVAMC which is designed to track in real-time treatment time periods and trigger warnings for treatment delays. We expect to be able to generate quantifiable information from these data which could serve as a benchmark for development of data-driven clinical practice guidelines within our and other tertiary VA centers throughout the United States.

Fragmentation of HNSCC care has been associated with increased costs and poor clinical outcomes, further demonstrating the importance of integration of multi-modality treatment delivery into one single unit.<sup>30</sup> Prospective efforts at high-quality, high-resolution treatment delivery data collection are essential to improving oncologic outcomes for veterans with HNSCC and potentially the HNSCC patient population at large. Such efforts will require substantial institutional and extramural support, but we believe that now is the time for a concerted effort in this direction.

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