


## ORIGINAL RESEARCH

# Prolonged inpatient stay after upfront total laryngectomy is associated with overall survival

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**Abstract**

**Objectives:** To investigate factors and complications associated with prolonged inpatient length of stay (LOS) in patients who receive total laryngectomy (TL), and to analyze its effect on short-term and long-term overall survival (OS).

**Methods:** The National Cancer Database (NCDB) was queried from 2004 to 2016 for patients with laryngeal cancer, who received TL within 60 days of diagnosis, and who had an inpatient LOS  $\geq 1$  night. Multivariable binary logistic regression and survival analyses on propensity score matched cohorts with Kaplan-Meier analysis and extended Cox regression were utilized.

**Results:** Eight thousand two hundred and ninety-eight patients from the NCDB were included. Median inpatient LOS was 8 days after TL (IQR: 7, 12). Prolonged LOS was defined as above the 75th percentile or 13 days or greater. On multivariable analysis, increasing patient age (OR 1.14 per 10 years,  $P = .003$ ), female sex (OR 1.35,  $P < .001$ ), and Charlson-Deyo comorbidity score of  $\geq 2$  compared to a score of 0 (OR 1.43,  $P < .001$ ) were associated with prolonged LOS. Patients treated at high surgical case volume centers had a decreased likelihood for prolonged LOS (OR 0.67,  $P < .001$ ). Ninety-day mortality increased over time in patients who stayed  $\geq 13$  days. Prolonged LOS was independently associated with worse OS on multivariable analysis (HR 1.40, 95% CI: 1.22, 1.61) in a matched cohort.

**Conclusions:** Prolonged LOS after TL serves as a strong indicator for postoperative long-term mortality and may help identify patients who warrant closer surveillance.

**Level of Evidence:** 3.

**KEYWORDS**

inpatient length of stay, laryngeal neoplasm, NCDB, survival, total laryngectomy

## 1 | INTRODUCTION

Since the Veterans Affairs' (VA) Larynx Trial in 1991, which demonstrated 2-year overall survival (OS) equivalence and the possibility for

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laryngeal preservation in patients treated with chemotherapy (CT) and radiation therapy (RT) compared to surgery, the use of upfront total laryngectomy (TL) as definitive therapy for laryngeal cancer has decreased dramatically.<sup>1,2</sup> In fact, TL is now being increasingly performed as a “salvage” operation after an initial failure of chemoradiation therapy (CRT).<sup>3,4</sup> However, per the NCCN guidelines, upfront TL continues to be suggested for patients with locally advanced disease, in whom laryngeal preservation is unlikely to be obtained with nonsurgical management (eg, T4a disease).<sup>5</sup>

As the utilization of TL has declined, more patients are being treated by high volume providers.<sup>6</sup> In all TL cases, as part of definitive management or salvage, the use of free flaps, inpatient length of stay (LOS), and postoperative complications have increased over the past 15 years in TL patients.<sup>2</sup> Inpatient LOS is a major contributor to health care costs,<sup>7</sup> and is a predictor of complications in complex operations such as TL.<sup>8</sup> Specifically, prolonged inpatient LOS has been associated with increased hospitalization cost and higher risk for nosocomial infection.<sup>9,10</sup>

To date, there have been many studies investigating short-term morbidity and mortality associated with head and neck cancer surgeries, including TL. Such studies have investigated factors associated with need for reoperation,<sup>11,12</sup> 30-day unplanned readmission,<sup>13-18</sup> 30-day mortality,<sup>19</sup> and prolonged inpatient LOS. Those investigating LOS include reviews of institutional<sup>20</sup> and national database.<sup>16,19,21</sup> Use of the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) to find associations with inpatient LOS have revealed that patients with increasing age, recent congestive heart failure exacerbation, totally dependent functional status, and African American race were independent risk factors for prolonged LOS.<sup>16,19</sup> Furthermore, the most common complication after TL in patients with reconstruction was wound infection (15.6%).<sup>19</sup> Wound infection and pharyngocutaneous fistula are associated with higher rates of unplanned readmission within 30-days of discharge.<sup>16,18</sup> Finally, use of the National Inpatient Sample database has demonstrated that high-volume facilities have lower rates of complications and shorter LOS in patients undergoing laryngectomy.<sup>21</sup>

Although previous studies have characterized certain factors associated with prolonged inpatient LOS, none have investigated differences in complications or assessed long-term survival outcome measures for these patients. Moreover, none have distinguished between primary vs salvage laryngectomy. We use the National Cancer Database (NCDB) to test the hypotheses that differences in demographic, clinical and oncologic factors are associated with prolonged inpatient LOS, and that prolonged LOS is independently associated with worse short-term and long-term OS in patients who receive upfront TL.

## 2 | MATERIALS AND METHODS

This work was exempted from IRB review by the Yale Human Research Protection Program.

### 2.1 | Patient selection

The NCDB was queried from 2004 to 2016 for patients with laryngeal cancer (C32.0-C32.9) who received TL or pharyngolaryngectomy (TPL) (surgery codes 40-50) within 60 days of diagnosis. Patients with inpatient LOS of 0 days or distant metastatic disease were excluded. Staging was based on the American Joint Committee on Cancer (AJCC) sixth or seventh editions. Time from surgery to RT and to CT were log-transformed with successful normalization of frequency distributions.

Information coded in the NCDB is done by trained Certified Tumor Registrars, and data undergoes extensive quality controls.<sup>22</sup> All cases were analytic, and all therapies included in the NCDB are part of a patient's first course of therapy. Duplicate cases are identified by the NCDB and each patient is only included once in the NCDB.

### 2.2 | Statistics

Statistical analysis was performed in SPSS versions 25 and 26 (IBM, Armonk, New York) and in SAS version 9.4 (SAS Institute, Inc, Cary, North Carolina). All statistics, where appropriate, were conducted at an  $\alpha = .05$  and were 2-tailed.

Prolonged inpatient LOS was defined as greater than the 75th percentile of inpatient LOS of patients who stayed at least one night. Differences in patient characteristics were determined by t-tests, Fisher's exact tests, and chi-squared analyses. Odds for prolonged hospitalization were assessed using a multivariable binary logistic regression run using a forward stepwise approach, with subsequent inclusion of covariates tested by Wald statistic at a  $P < .05$ .

Long-term OS was assessed in a propensity score (PS) matched cohort. Factors included in the PS calculation can be found in the balance assessment (Supporting Information Table S1). All patients had squamous cell carcinoma (histology codes 8070-8078). PS matching was performed using the next-neighbor greedy method in a 1:1 fashion with a caliper of 0.15 for the PS. Receipt of immunotherapy, receipt of adjuvant CT, and receipt of adjuvant RT were not included in the PS calculation, but were rather exactly matched on. We additionally exactly matched on age by 10-year interval and Charlson-Deyo comorbidity score to improve balance on key factors that were, a priori, believed to be associated both with patient overall health and postoperative survival. The two cohorts were well balanced as assessed using standardized mean differences.<sup>23</sup>

Survival analysis was performed to assess short-term and long-term survival outcomes. Ninety-day mortality was performed on the unmatched cohort. To address immortal time bias,<sup>24</sup> long-term OS was assessed in patients who survived at least 3 months from surgery, as calculated by months to surgery subtracted from months to last follow-up or death since diagnosis. Survival analysis was performed using Kaplan-Meier analysis and extended Cox proportional hazard regression. Deviation from proportional hazards was assessed through correlation of Schoenfeld's residuals over ranked time in a multivariable model. Age ( $P = .043$ ), clinical N2c disease ( $P = .001$ ) relative to

NO, and receipt of  $\geq 60$  Gy RT dose ( $P = .029$ ) relative to  $< 44$  Gy all statistically violated proportional hazards. A final extended regression model, including linear time-dependent covariates for the three aforementioned covariates was included in a final extended model.

A post hoc analysis was also performed using the Surveillance, Epidemiology, and End Results (SEER) Program from 2004 to 2016 to assess laryngeal cancer disease-specific survival (DSS). Patients were selected for using similar criteria used for the NCDB cohort, which was only limited by differences in information encoded in the respective datasets. LOS and time from diagnosis to surgery are not captured in the SEER, so were not included. All therapy in the SEER is primary therapy, and all patients received TL. A competing risks survival analysis with the Fine and Gray model was used.

### 3 | RESULTS

We identified 8298 patients in the NCDB for inclusion into the study. The median inpatient LOS after upfront TL was 8 days (IQR: 7, 12) (Figure 1). We therefore defined “prolonged” inpatient LOS as  $> 75$ th percentile, or 13 days or longer.

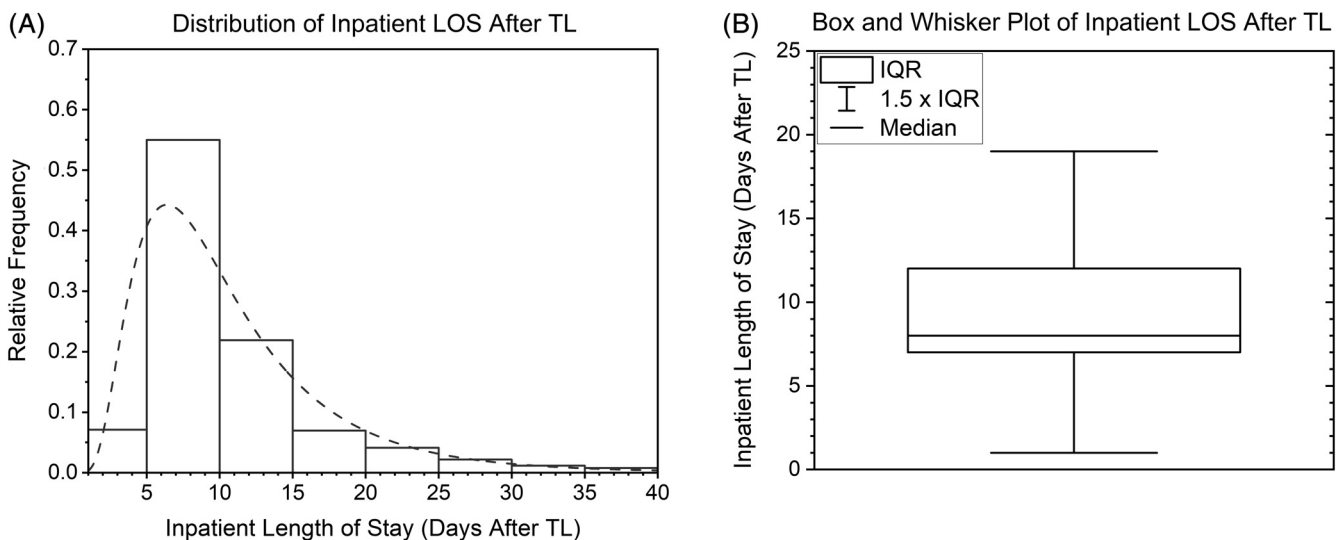
To test the hypothesis that there are demographic, clinical and oncologic factors associated with, and predictive of prolonged LOS, we compared patient and hospital factors using simple and multivariable analyses (Table 1). On multivariable analysis, demographic factors associated with prolonged inpatient LOS (Table 1) included increasing age (odds ratio [OR] 1.14 per decade, 95% CI: 1.04, 1.23), female sex (OR 1.35, CI: 1.15, 1.59), nonwhite race ( $P = .001$ ), and Charlson-Deyo comorbidity score of  $\geq 2$  compared to 0 (OR 1.43, 1.17, 1.75). Patients with Medicare (OR 0.80, CI: 0.66, 0.97) and Medicaid or uninsured (OR 0.70, CI: 0.58, 0.84) were less likely than those with private insurance to have prolonged hospitalizations. Geographic factors such as

region within the United States and urban-rural continuum were also associated with inpatient LOS. Finally, in terms of clinical and oncologic factors, patients treated at hospitals with high TL-specific volume ( $> 5$  cases per year) were less likely to have prolonged hospitalization (OR 0.67, CI: 0.55, 0.80), whereas patients who had positive margins (OR 1.35, CI: 1.11, 1.64) or TPL as opposed to TL (OR 1.45, CI: 1.18, 1.78) were more likely to have prolonged hospitalization. Clinical T and N stages and tumor primary site were not associated with LOS on multivariable, adjusted analysis. Prolonged hospitalization is associated with delays in receipt of adjuvant RT (mean 8.4 days,  $P < .001$ ) and CT (mean 10.1 days,  $P < .001$ ).

#### 3.1 | Association between inpatient length of stay and short-term and long-term overall survival

To address the final hypothesis that complications experienced in the hospital may lead to worse short-term and long-term survival, we used the NCDB to assess both 90-day mortality (Figure 2A) and OS in patients who survival  $\geq 3$  months from surgery (Figure 2B). In terms of 90-day mortality, we observed the lowest mortality rate in patients who stay 5 to 8 days (2.6%, CI: 2.1, 3.2%). Ninety-day mortality increases linearly in patients who stay  $\geq 13$  days to a rate of 13.5% (CI: 9.6, 17.3%) in patients who stay 29 to 90 days in the hospital. Across all patients staying  $\leq 90$  days, the average 90-day mortality after primary TL was 4.3% (CI: 3.8, 4.7).

To address long-term survival, we performed a combined 1:1 propensity score and exact matching based on patient demographic, clinical, and oncologic factors with good balancing of covariates in the matched cohort (Supporting Information Table S1). On Kaplan-Meier analysis of the matched cohort of patients who survived  $\geq 3$  months (721 in each arm), patients who had prolonged inpatient LOS had a



**FIGURE 1** Distribution of inpatient length of stay (LOS) after total laryngectomy in patients who stayed at least 1 day. A, Data shown through 40 days in accordance with the NCDB Data Use Agreement. Dashed line represents a lognormal distribution. IQR, interquartile range; TL, total laryngectomy

**TABLE 1** Description of patient characteristics (left) and multivariable binary logistic regression (right) evaluating factors associated with prolonged inpatient length of stay after total laryngectomy (≥13 days) adjusted for patient, environmental, and clinical factors

	LOS 1-12 days	LOS ≥13 days	P	Odds ratio (95% CI)	P
<i>Patient factors</i>					
Age (mean, SD; per 10 years)	61.6 (10.3)	62.7 (10.6)	<.001	1.14 (1.04, 1.23)	.003
Sex					
Male	5192 (81.2%)	1494 (78.5%)	.008	Ref.	
Female	1202 (18.8%)	410 (21.5%)		1.35 (1.15, 1.59)	<.001
Race					
White	5185 (81.8%)	1425 (75.8%)	<.001	Ref.	
Black	1046 (16.5%)	401 (21.3%)		1.37 (1.15, 1.63)	<.001
All else	110 (1.7%)	54 (2.9%)		1.33 (0.86, 2.04)	.20
Hispanic origin					
No	5791 (95.5%)	1681 (93.6%)	.001	Ref.	
Yes	272 (4.5%)	115 (6.4%)		1.42 (1.06, 1.90)	.020
Charlson-Deyo score					
0	3843 (60.1%)	1054 (55.4%)	<.001	Ref.	
1	1885 (29.5%)	582 (30.6%)		1.07 (0.92, 1.24)	.38
2+	666 (10.4%)	268 (14.1%)		1.43 (1.17, 1.75)	<.001
Insurance status					
Private	1779 (28.3%)	569 (30.4%)	<.001	Ref.	
Medicare	2571 (41.0%)	853 (45.6%)		0.80 (0.66, 0.97)	.020
Medicaid or uninsured	1838 (29.3%)	421 (22.5%)		0.70 (0.58, 0.84)	<.001
Other	89 (1.4%)	27 (1.4%)		1.29 (0.72, 2.22)	.36
<i>Environmental factors</i>					
Geographic location					
Central	3301 (52.2%)	819 (43.5%)	<.001	Ref.	
New England	191 (3.0%)	79 (4.2%)		1.86 (1.32, 2.61)	<.001
Mid-Atlantic	749 (11.8%)	321 (17.0%)		1.54 (1.26, 1.88)	<.001
South Atlantic	1514 (24.0%)	447 (23.7%)		1.17 (0.99, 1.38)	.073
Mountain	164 (2.6%)	57 (3.0%)		1.39 (0.93, 2.09)	.11
Pacific	405 (6.4%)	161 (8.6%)		1.53 (1.19, 1.98)	.001
Location type					
Metropolitan	4570 (72.8%)	1470 (78.7%)	<.001	Ref.	
Urban	1505 (24.0%)	367 (19.7%)		0.98 (0.84, 1.16)	.84
Rural	206 (3.3%)	30 (1.6%)		0.50 (0.31, 0.81)	.005
<i>Clinical/oncologic factors</i>					
Clinical T stage					
T1	190 (3.9%)	44 (3.1%)	.025		>.05
T2	485 (10.0%)	148 (10.4%)			
T3	1791 (37.1%)	491 (34.4%)			
T4a	2338 (48.4%)	728 (51.0%)			
T4b	29 (0.6%)	17 (1.2%)			
Clinical N stage <sup>a</sup>					
N0	64.7%	61.9%	.34		>.05
N1	12.5%	13.1%			
N2a	1.3%	1.4%			
N2b	9.1%	9.8%			
N2c	11.7%	13.3%			
N3	0.8%	0.6%			

(Continues)

**TABLE 1** (Continued)

	LOS 1-12 days	LOS ≥13 days	P	Odds ratio (95% CI)	P
Tumor site					>.05
Glottis	1962 (30.7%)	520 (27.3%)	.012		
Supraglottis	2399 (37.5%)	730 (38.3%)			
Other or overlapping sites	2033 (31.8%)	654 (34.4%)			
Surgical volume of center					
<1 case per year	1622 (25.4%)	536 (28.2%)	<.001	Ref.	
1-5 cases per year	2701 (42.2%)	900 (47.3%)		1.01 (0.85, 1.20)	.91
>5 cases per year	2071 (32.4%)	468 (24.6%)		0.67 (0.55, 0.80)	<.001
Facility type					>.05
Nonacademic	2287 (36.2%)	708 (37.6%)	.26		
Academic	4037 (36.2%)	1176 (62.4%)			
Margin status					
Negative	5570 (88.7%)	1589 (84.7%)	<.001	Ref.	
Positive	713 (11.3%)	288 (15.3%)		1.35 (1.11, 1.64)	.002
Surgery performed					
Total laryngectomy	5777 (90.4%)	1665 (87.4%)	.005	Ref.	
Pharyngolaryngectomy	617 (9.5%)	239 (12.6%)		1.45 (1.18, 1.78)	<.001

<sup>a</sup>Total counts cannot be shown per NCDB Data User Agreement.

median survival of 38.0 months (CI: 32.4, 43.8) compared to 55.3 months (CI: 47.9, 65.4) in those with shorter inpatient LOSs (log-rank  $P < .001$ ) (Figure 2B). Survival curves begin to reconverge after approximately 72 months (6 years), so a post hoc Breslow-Wilcoxon test was also performed ( $P < .001$ ).

On extended multivariable Cox proportional hazard regression (Table 2), prolonged inpatient LOS after TL was associated with an increased risk for death (hazard ratio [HR] 1.40, CI: 1.22, 1.61). Other factors associated with an increased hazard for death include increasing age (HR 1.16 per 10 years, CI: 1.03, 1.31), advanced clinical nodal disease ( $P < .001$ ) and positive margins (HR 1.60, CI: 1.30, 1.96). Receipt of full-dose adjuvant RT was associated with improved OS compared to patients who received <44 Gy (HR 0.72, CI: 0.55, 0.94). Insurance status was adjusted for but not associated with OS in our model ( $P = .30$ ). In a post hoc analysis of patients who received adjuvant RT, delay in start of RT from surgery by 8 weeks was not associated with OS ( $P = .37$ ).

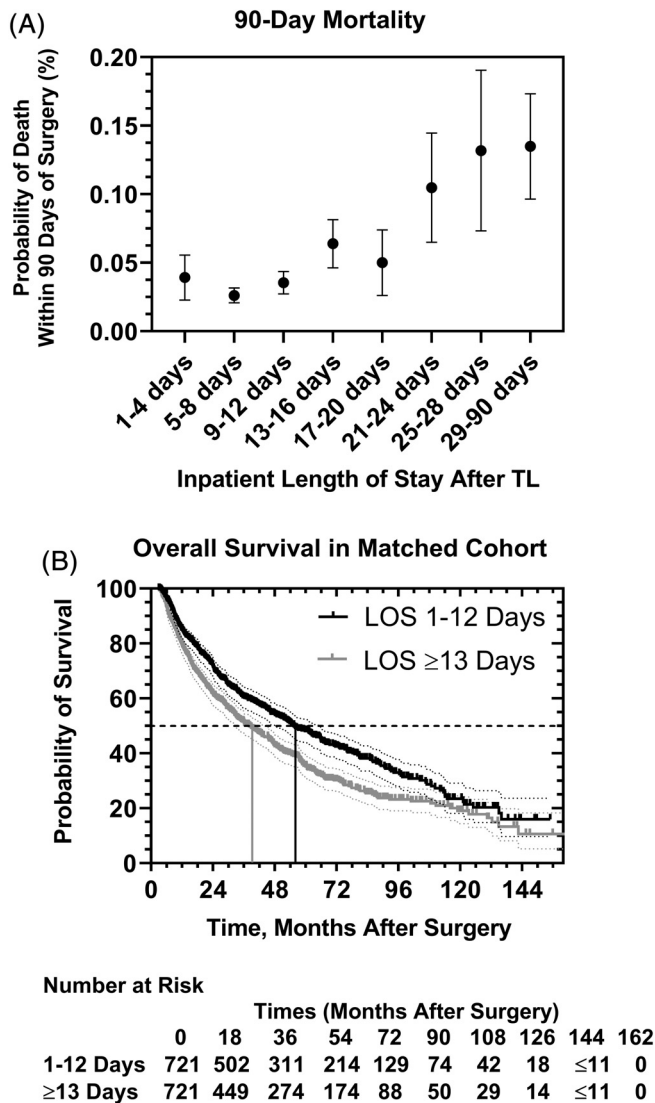
Finally, to assess whether the increased risk for death associated with prolonged LOS was due to recurrence, the SEER database was queried to measure OS and DSS. In patients who survived at least 3 months from diagnosis, the median OS in the SEER cohort was 48.0 months (CI: 45.0, 52.0), which was compared to the pooled OS in the NCDB of 51.6 months (CI: 48.5, 54.1) (Figure 3A). The highest probability of death from laryngeal cancer peaks at 12 months after TL, in which 55.9% of deaths are attributable to the disease. By 36 months, DSS begins to plateau (Figure 3B).

## 4 | DISCUSSION

Utilization of upfront TL for curative intent in patients with laryngeal cancer is associated with long-term morbidity, primarily associated with quality of life and loss of laryngeal functions. However, the long-term associations of perioperative morbidity and long-term survival have not been previously studied. In this report, we highlight that a surrogate marker for perioperative morbidity, namely prolonged inpatient LOS, is associated with statistically and clinically worse short-term and long-term OS in a matched cohort of patients treated with upfront TL for laryngeal cancer.

Previous studies that have examined prolonged inpatient hospitalization after TL have been limited to short-term follow-up information, such as 30-day readmission, need for return to the OR, and short-term mortality.<sup>16,18,19,21</sup> These studies have used datasets, such as the NSQIP and National Inpatient Sample,<sup>16,21</sup> that have advantages for short-term endpoints, but do not contain the oncologic information or long-term follow-up information encoded by a dataset such as the NCDB. Given the nature of the NCDB, there are theoretically no salvage TL cases or previously irradiated necks included in our analysis.

Our most notable finding was that prolonged hospitalization after TL is associated with worse long-term OS. To the best of our knowledge, this is the first published study to show this finding. Our results suggest inpatient LOS is independently more strongly associated with long-term OS than comorbidity score or even adjuvant CT. We should underscore that in interpreting this data, we do not believe that the



**FIGURE 2** Association of length of hospital stay with A, 90-day mortality after surgery and B, overall survival past 90 days. A, Error bars represent 95% confidence intervals. B, Kaplan-Meier analysis was performed on the matched cohort. Dashed line indicates 50% survival with corresponding solid drop lines corresponding to median survival times. Dotted lines represent 95% confidence intervals. LOS, inpatient length of stay; TL, total laryngectomy

physical act of staying longer in the hospital affects long-term survival, but rather that perioperative complications beget complications down the line of recovery. We show, using the SEER database, that disease-specific mortality starts to markedly diverge from overall mortality at approximately 36 months, whereas survival differences between patients who experience shorter and prolonged LOSs start to reconverge after approximately 72 months. This discrepancy highlights that the increased risk for death in the cohort of patients who experience prolonged LOS cannot entirely be explained by recurrence of disease. Therefore, survival differences are likely influenced by both disease-specific and medical morbidity and mortality. Finally, the interpretation that future complications may lead to more complications is

plausible, as it has already been described that complications, such as anemia, may lead to further complications, such as pharyngocutaneous fistula development.<sup>25</sup>

In assessing long-term survival, we also describe that although prolonged LOS was associated with delayed receipt of adjuvant therapy, there was no association between that delay and OS in the matched cohort. This finding does not agree with a previous analysis of patients with laryngeal cancer, which showed an association between worse OS and delays in time from surgery to RT at the 8-week mark.<sup>26</sup> This may be due to selection for patients who survived ≥3 months in the long-term survival analysis or due to unique patient and clinical factors associated with the cohort of patients who are selected for upfront TL. This heterogeneity in patient disease is supported by the finding that treatment delay, in terms of time from surgery to RT, is associated with OS in some head and neck cancers but not others.<sup>27-29</sup>

The short-term results that we describe in the study, such as the decreased likelihood for patients to have prolonged hospitalizations at high case volume centers and the increased LOS in black patients, is in agreement with previous publications.<sup>16,21</sup> We expand on these findings, through the use of institutional data encoded in the NCDB, and show that environmental factors such as geographic location and location type (metropolitan vs rural) may impact inpatient LOS. It is interesting that patients with Medicare and Medicaid or who were uninsured were less likely to have prolonged inpatient LOS. It is possible that hospital coordinators work more aggressively to discharge these patients due to limitations on number of inpatient hospital days allowed by Medicare.<sup>30</sup> Although those on Medicare or Medicaid are less likely to have prolonged LOS in our study, insurance status was not independently associated with OS. Furthermore, previous research has shown that these insurance status groups may be at higher risk for hospital readmission<sup>15,31</sup> and all-cause mortality.<sup>26</sup> Future research should be dedicated to understanding this finding.

Although we assessed long-term OS, we caution that our results cannot be correlated with long-term follow-up data from the RTOG 91-11 trial.<sup>4</sup> The Kaplan-Meier analysis was performed on a matched cohort that selected for patients who were older in age, had higher comorbidity scores, and had positive margins after TL. Our study was not designed to assess differences between upfront CRT therapy vs TL, and a conclusion from such a hypothetical comparison cannot be answered by results from this study. Nonetheless, when considering the long-term follow-up data from the RTOG 91-11 trial,<sup>4</sup> we also highlight that there may be an increasing role for upfront TL. That is, the follow-up results demonstrated that patients treated with concomitant CT/RT had a decline in long-term OS that was not attributable to a patient's cancer diagnosis. This late-term toxicity that was not well characterized in the original study.<sup>3</sup>

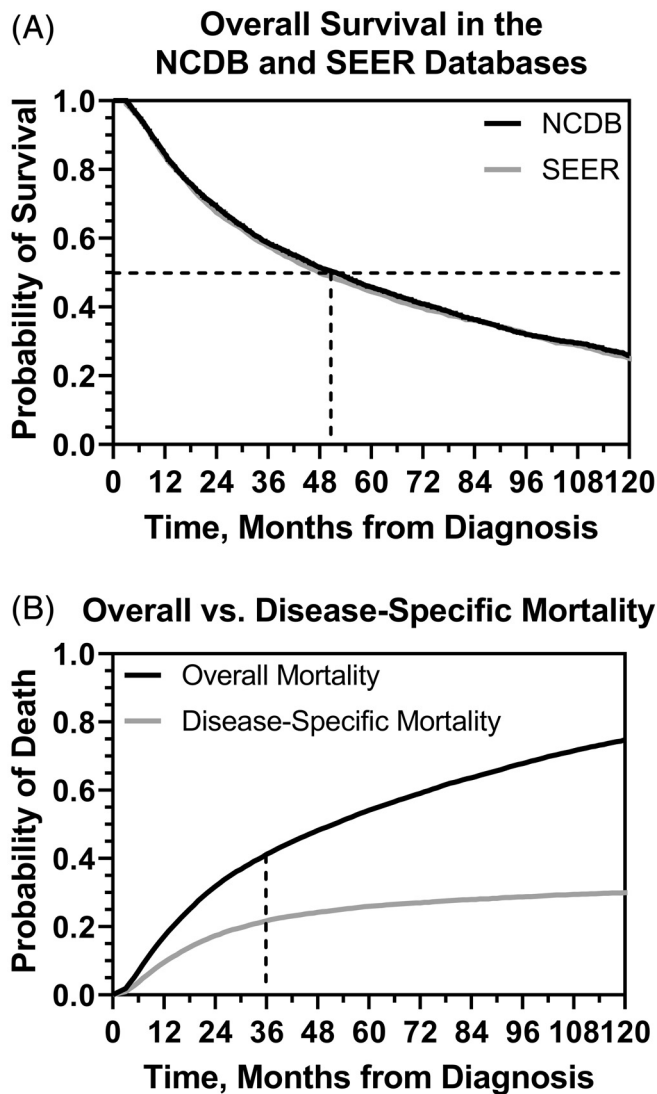
The study has the potential to guide clinical practice through multiple lenses. First, inpatient LOS is not a fixed factor, and can be modified through optimization of postoperative care. Although our results are associations, it is possible that aggressive strategies to minimize and/or rapidly treat postoperative complications such as venous thromboembolism, pneumonia, surgical site infections and anemia

**TABLE 2** Extended multivariable Cox regression evaluating factors associated with overall survival after total laryngectomy in a combined 1:1 propensity score and exactly matched cohort

	HR (95% CI)	P
<i>Patient factors</i>		
Age (per 10 years)	1.16 (1.03, 1.31)	.016
Age (time dependent, per 10 years)	1.00 (1.00, 1.01)	.025
Sex		
Male	Ref.	
Female	0.80 (0.67, 0.96)	.014
Race		.52
Hispanic origin		.98
Charlson-Deyo score		.35
Insurance status		.30
<i>Environmental factors</i>		
Geographic location		.37
Location type		.84
<i>Clinical/oncologic factors</i>		
Clinical T stage		.29
Clinical N stage		
N0	Ref.	
N1	1.20 (0.98, 1.48)	.081
N2a	1.90 (1.13, 3.20)	.015
N2b	1.55 (1.21, 1.99)	.001
N2c	1.88 (1.33, 2.66)	<.001
N3	1.43 (0.45, 4.55)	.54
Clinical N stage (time dependent)		
N0		
N2c	0.99 (0.98, 1.00)	.036
Tumor site		.61
Surgical volume of center		.36
Facility type		
Nonacademic	Ref.	
Academic	1.25 (1.04, 1.50)	.020
Margin status		
Negative	Ref.	
Positive	1.60 (1.30, 1.96)	<.001
Surgery performed		.32
Adjuvant chemotherapy		.44
Adjuvant radiation dose		
0-4399 cGy	Ref.	
4400-5999 cGy	0.93 (0.74, 1.17)	.53
≥6000 cGy	0.72 (0.55, 0.94)	.014
Adjuvant radiation dose (time dependent)		.081
Inpatient length of stay		
1-12 days	Ref.	
≥13 days	1.40 (1.22, 1.61)	<.001

Notes: Hazard ratios (HR) for factors with *P*-values >.05 are not provided given lack of statistical significance, but are adjusted for in the multivariable model.





**FIGURE 3** A, Comparison of overall survival in the National Cancer Database (NCDB) and the Surveillance, Epidemiology, and End Results Program (SEER) databases. B, Comparison of overall and disease-specific mortalities in patients receiving total laryngectomy in the SEER

may lead to better long-term survival outcomes. Second, LOS is a defined characteristic that is easily obtainable from the patient record and may serve as a prognostic indicator that is strongly correlated with patient outcome. Just as clinicians use other prognostic markers to conceptually understand the expected oncologic course, a clinically meaningful prognostic marker such as LOS can inform clinician understanding and guide surveillance strategies. For instance, patients who experienced a prolonged inpatient LOS may be more closely followed, more aggressively managed in the event of future complications or concern for disease recurrence, and appropriately counseled. Finally, prolonged inpatient LOS may be an important covariate to include as a proxy for perioperative morbidity in future clinical research.

One limitation of this study is the lack of coding of specific comorbidity codes or comorbidities in the NCDB or the SEER

databases. Although the Charlson-Deyo comorbidity score captures medical comorbidity, there is no marker of patient frailty. Indeed, frailty has been associated with increased complications and death attributable to surgery.<sup>32</sup> “Prehabilitation,” or the act of carefully selecting suitable surgical candidates and optimizing their preoperative health through a multidisciplinary approach, may result in shorter inpatient LOS and improved outcomes.<sup>33,34</sup>

Another limitation of our analysis was selection bias. To address such bias associated with prolonged hospitalization, we utilized a combined propensity score and exactly matched cohort design to assess long-term survival. This method reduces the likelihood of one cohort having a higher risk profile for death than the other cohort; thus, allowing for us to more clearly demonstrate an independent association of LOS with OS. Furthermore, to address immortal time bias, in which patients die before receiving recommended therapy, long-term survival was assessed starting 3 months after surgery.<sup>24</sup> Finally, we could not assess cause of death or recurrence-free survival in the NCDB, which would be important endpoints to assess in future multi-institutional retrospective studies or prospective studies.

## 5 | CONCLUSION

Prolonged inpatient LOS after upfront TL for laryngeal cancer is associated with worse long-term OS, which suggests that perioperative complications beget future complications. These findings may be used to inform quality improvement efforts and clinical management, from preoperative patient counseling and risk stratification to postoperative prevention and treatment of complications.

## ACKNOWLEDGMENTS

The data used in the study are derived from a deidentified NCDB file. The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

## CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

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## SUPPORTING INFORMATION

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

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