Neck dissection does not add to morbidity or mortality of laryngectomy

Christopher C. Xiao, Sarah A. Imam, Shaun A. Nguyen, Marc P. Camilon, Andrew B. Baker, Terry A. Day, Eric J. Lentsch

Department of Otolaryngology-Head and Neck Surgery, Kaiser Permanente, Northern California, Oakland, CA, 94612, USA

Department of Health and Human Performance, The Citadel, Charleston, SC, 29409, USA

Department of Otolaryngology-Head and Neck Surgery, Medical University of South Carolina, Charleston, SC, 29425, USA

Oregon Health & Science University Ear, Nose & Throat, Portland, OR, 97239, USA

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Abstract: Objectives: To examine the national rates of complications, readmission, reoperation, death and length of hospital stay after laryngectomy. To explore the risks of neck dissection with laryngectomy using outcomes.

Methods: The American College of Surgeons National Quality Improvement Program (ACS-NSQIP) database was reviewed retrospectively. The database was analyzed for patients undergoing laryngectomy with and without neck dissection. Demographic, perioperative complication, reoperation, readmission, and death variables were analyzed.

Results: 754 patients who underwent total laryngectomy during this time were found. Demographic analysis showed average age was 63 years old, 566 (75.1%) were white, and 598 (79.3%) were male. Of these patients, 520 (69.0%) included a neck dissection while 234 (31.0%) did not.

When comparing patients who received a neck dissection to those who did not, there were no significant differences in median length of hospital stay (12.5 days vs. 13.3 days, \( P = 0.99 \)), rates of complication (40% vs. 35% w/o, \( P = 0.23 \)), reoperation (13.5% w/ vs. 14% w/o, \( P = 0.81 \)), readmission (14% w/ vs. 18% w/o, \( P = 0.27 \)), and death (1.3% w/ vs. 1.3% w/o, \( P > 0.99 \)). Furthermore, neck dissection did not increase the risk of complication.

* Corresponding author. 135 Rutledge Ave, MSC 550, Charleston, SC, 29425, USA. Fax: +1 843 792 0546.

E-mail address: nguyensh@musc.edu (S.A. Nguyen).

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Introduction

It has been well established that cervical lymph node metastasis is one of the most important prognostic factors in laryngeal cancer.\(^1\text{-}^5\) For this reason, neck dissection has been found to be an effective option in the treatment of primary laryngeal cancers.\(^6\text{-}^9\) Indeed, treatment guidelines recommend neck dissection with laryngectomy for therapeutic and staging purposes in most patients with large tumors in order to identify occult nodal metastases that influence prognosis.\(^4\text{-}^10\) However, starting in the early 1990s, the treatment of laryngeal cancer has changed dramatically, making it more difficult to assess the actual outcomes of neck dissection. Studies showing equivalent outcomes between chemoradiation and laryngectomy has greatly increased larynx preserving approaches.\(^11\text{-}^14\) Laryngectomy is performed commonly as a salvage procedure after failure of organ preserving therapy.\(^12\text{-}^15\) Since laryngectomy is performed less, and in a different set of patients who are post-chemoradiation, there is concern that the benefits of concurrent neck dissection may no longer outweigh the potential complications.\(^7\text{-}^16\text{-}^18\) It is important to get an accurate understanding of the peri-operative outcomes and complications of neck dissection in laryngectomy to determine if the benefits outweigh the risks.

A major limitation in recent studies in this matter lies in the sample size available for analysis. Most studies are limited to single institutions and have small numbers of patients, making it difficult to assess complication rates of laryngectomy with neck dissection compared to those without. The American College of Surgeons’ National Surgical Quality Improvement Program (ACS-NSQIP) database was designed to track outcomes following surgery, and collects data from over 200 hospitals starting from 2005.\(^19\) This nationwide, multi-institutional database provides the largest, recent sample of laryngectomy patients and outcomes, which will allow us to better understand the effect of neck dissection on complication rates in laryngectomy. Therefore, we chose to use the NSQIP database to determine if the addition of neck dissection increased complication rates or length of stay in total laryngectomies.

Materials and methods

Data source

The ACS-NSQIP is a nationally validated, prospective, multi-institutional database that provides risk-adjusted patient specific surgical outcomes data. ACS-NSQIP data is available to participating hospitals and affiliated individuals throughout the United States. ACS-NSQIP details more than 300 data points for de-identified cases including preoperative comorbidities and demographic information, intraoperative variables, and 30-day postoperative outcomes. The Medical University of South Carolina Institutional Review Board has determined that this project meets criteria for ‘Not Human Subjects’ research.

Patient identification

We performed a retrospective analysis using the ACS-NSQIP databases for the years 2005–2012. The Current Procedural Terminology (CPT) codes for laryngectomy are categorized by extent of resection and concomitant neck dissection. Patients were identified using the definitive procedure codes for total laryngectomy [CPT: total laryngectomy (31360, 31365)]. To ensure a consistent base cohort of patients, this project focused only on patients undergoing total laryngectomy. The patients were separated into groups based on whether they underwent a concurrent neck dissection utilizing corresponding CPT codes: 31368, 31365, 38720, and 38724. Patients that were \(\geq 90\) years old were excluded due to ACS-NSQIP coding of these patients as \(\geq 90\) (Fig. 1).

Thirty-day postoperative outcomes

Patients were separated into groups based on whether they underwent a concurrent neck dissection. Variables
compared between groups included demographics (age, race, gender), comorbidities (current smoker within 1 year, history of severe chronic obstructive pulmonary disorder (COPD), previous percutaneous coronary intervention (PCI), hypertension (HTN) requiring medication, >10% loss body weight in last 6 months, dyspnea, metastatic cancer), and operative characteristics [prior operation within 30 days, pre-operative serum sodium, pre-operative serum blood urea nitrogen (BUN), pre-operative serum creatinine, pre-operative serum albumin, pre-operative white blood cell count (WBC), pre-operative hematocrit, pre-operative international normalized ratio (INR)]. Operative characteristics evaluated included American Society of Anesthesiologists (ASA) classification and whether the patient had concurrent reconstructive surgery, identified using CPT codes for pectoralis flap or free flap reconstruction (15732, 15756, 15757, 15758).

Frequency of complications in the 30-day post-operative period was evaluated. Complications included superficial surgical site infection, deep surgical site infection, wound dehiscence, and graft/prosthesis/flap failure, cardiovascular (cardiac arrest, myocardial infarction, or stroke), pulmonary (pneumonia, unplanned re-intubation, or ventilator-assisted respiration for more than 48 h), neurologic (coma or peripheral nerve damage), renal (progressive renal insufficiency or acute renal failure), thromboembolic (deep vein thrombosis or pulmonary embolism), urinary tract infection, bleeding complication requiring blood transfusion, and sepsis or septic shock. Separate analyses were performed for factors predicting any complication, readmission, reoperation, death, and total length of hospital stay.

Statistical analysis

All analyses were performed with SPSS 22.0 and Sample Power 3.0 (IBM Corporation, Armonk, NY). Categorical variables are presented as frequency and percentage, and continuous variables are presented as mean ± standard deviation or as mean and range in text and tables. All continuous variables were assessed for normality using Q–Q plots. If these variables were not normally distributed, descriptive measurements such as median and interquartile range (IQR) were calculated. Comparisons of patient characteristics were performed using a Chi-square test or Fisher’s exact test for categorical variables and an independent t test or a Mann–Whitney rank sum test for continuous variables. A correlation model was used to determine the relationship between the independent variables (demographic, comorbidities, operative characteristics) and dependent outcome variables (complications, reoperation, readmission, and length of stay). All independent variables that showed a significant correlation (0.05) with dependent variables were compared between groups by concurrent neck dissection and placed in univariate and multivariate logistic regression or linear regression models. The adjusted odds ratio (OR) or unstandardized B coefficient and its confidence interval (CI) and P-value were obtained from the final model as a measure of the association between the independent predictors and the dependent responses. Power analyses at the probability level of 0.05 were done for proportions (2-tailed) where a sample size of 95 would yield 80% power, t-tests (2-tailed) with a mean difference of 1.0 ± 11.0 where a sample size of 1901 would yield 80% power, and multiple regression (medium effect size of 0.15) with four independent predictors where a sample size of 84 would yield 80% power. A P value of <0.05 was considered to indicate a statistically significant difference for all statistical tests.

Results

A total of 754 cases of total laryngectomy were identified, with a mean age of (63 ± 11) years with a range of 20–88. The majority of our patients were male (79.3%) and white (75.1%). A total of 520 (69.0%) of patients underwent concurrent neck dissection with total laryngectomy, while 234 (31.0%) did not.

Other demographic variables were compared in the group of patients who underwent concurrent neck dissection to those who did not. We found that the group undergoing concurrent neck dissection had significantly more current smokers [273 (52.5%) vs. 82 (35.0%), P < 0.001], fewer patients with previous PCI [25 (8.3%) vs. 22 (14.6%), P = 0.04], and were significantly more likely to undergo concurrent reconstructive surgery [130 (75.6%) vs. 42 (24.4%), P = 0.04] than the group that did not have concurrent neck dissection. The other demographic variables and pre-operative lab values were similar between the two groups (Table 1).

Discussion

The National Comprehensive Cancer Network Guidelines recommend therapeutic neck dissection for palppable neck disease or radiologic evidence of neck metastasis in both primary laryngeal cancer and recurrence. In practice, the decision whether or not to perform a neck dissection (ND) is quite complex. The evidence supporting neck dissection to accompany primary laryngeal cancer surgery depends on the risk of neck metastasis versus the risk of complications. Regarding salvage total laryngectomy (TL), the risk of post-operative complications such as fistula formation is generally thought to be even greater than after primary surgery; however, additional factors affect the risk of neck disease, e.g. neck irradiation at the time of initial treatment. Schwartz et al reviewed over 2063 total laryngectomy cases with unilateral or bilateral neck dissections performed in 58.7% of cases, and found that neck dissection was not associated with wound complications defined as superficial wound infection, deep wound infection, wound dehiscence, or fistula. Despite having the largest sample size of any total laryngectomy study, their cohort was between 1991 and 1999. Furthermore, the authors did not focus specifically on neck dissection, but rather assessed many variable to determine if they were predictors of wound complication. Since then, the trend of treatment of primary laryngeal cancer has persisted towards larynx preserving management: endoscopic resection or radiation for early stage laryngeal cancer and concurrent chemotherapy with radiation for late stage laryngeal cancer.
the rate of total laryngectomy has fallen 48% from 1997 to 2008. Despite a decrease in the rate of total laryngectomy, the use of neck dissection has not changed significantly, from 10% in 1993–2000 to 13% in 2001–2008 ($P = 0.136$). At this time, there are two distinct groups of patients receiving surgical neck management, those with primary and those with recurrent laryngeal cancer. Since the landscape of laryngeal cancer treatment has continued to change after the cohort examined by Schwartz, the question of whether neck dissection adds an additional risk of complications to laryngectomy must be readdressed.

### Table 1: Demographics.

| Variables                              | All patients | No neck dissection | Neck dissection | $P$-value |
|----------------------------------------|--------------|--------------------|----------------|-----------|
| Age (year, Mean ± SD)                  | 63 ± 11      | 63 ± 2             | 63 ± 11        | 0.82      |
| Race [n (%)]                           |              |                    |                |           |
| White                                  | 566 (75.1)   | 182 (77.8)         | 384 (73.8)     | 0.44      |
| Black                                  | 104 (13.8)   | 27 (11.5)          | 77 (14.8)      |           |
| Other                                  | 84 (11.1)    | 25 (10.7)          | 59 (11.3)      |           |
| Gender [n (%)]                         |              |                    |                |           |
| Female                                 | 156 (20.7)   | 52 (22.2)          | 104 (20.0)     | 0.49      |
| Male                                   | 598 (79.3)   | 182 (77.8)         | 416 (80.0)     |           |
| Current smoker within one year [n (%)] |              |                    |                |           |
| No                                     | 399 (52.9)   | 152 (65.0)         | 247 (47.5)     | <0.001    |
| Yes                                    | 355 (47.1)   | 82 (35.0)          | 273 (52.5)     |           |
| History of severe COPD [n (%)]         |              |                    |                |           |
| No                                     | 602 (79.8)   | 186 (79.5)         | 416 (80.0)     | 0.87      |
| Yes                                    | 152 (20.2)   | 48 (20.5)          | 104 (20.0)     |           |
| Previous PCI [n (%)]                   |              |                    |                |           |
| No                                     | 407 (89.6)   | 129 (85.4)         | 278 (91.7)     | 0.04      |
| Yes                                    | 47 (10.4)    | 22 (14.6)          | 25 (8.3)       |           |
| HTN requiring medication [n (%)]       |              |                    |                |           |
| No                                     | 381 (50.5)   | 127 (54.3)         | 254 (48.8)     | 0.17      |
| Yes                                    | 373 (49.5)   | 107 (45.7)         | 266 (51.2)     |           |
| >10% loss in body weight in last 6 months [n (%)] |       |                    |                |           |
| No                                     | 631 (83.7)   | 196 (83.8)         | 435 (83.7)     | 0.97      |
| Yes                                    | 123 (16.3)   | 38 (16.2)          | 85 (16.3)      |           |
| Dyspnea [n (%)]                        |              |                    |                |           |
| No                                     | 559 (74.1)   | 179 (76.5)         | 380 (73.1)     | 0.32      |
| Yes                                    | 195 (25.9)   | 55 (23.5)          | 140 (26.9)     |           |
| Metastatic cancer [n (%)]              |              |                    |                |           |
| No                                     | 662 (87.8)   | 206 (88.0)         | 456 (87.7)     | 0.89      |
| Yes                                    | 92 (12.2)    | 28 (12.0)          | 64 (12.3)      |           |
| Prior operation within 30 days [n (%)] |              |                    |                |           |
| No                                     | 399 (88.5)   | 134 (89.3)         | 265 (88.0)     | 0.68      |
| Yes                                    | 52 (11.5)    | 16 (10.7)          | 36 (12.0)      |           |
| ASA classification [n (%)]             |              |                    |                |           |
| I                                      | 2 (0.3)      | 1 (0.4)            | 1 (0.2)        | 0.79      |
| II                                     | 75 (10.0)    | 26 (11.1)          | 49 (9.5)       |           |
| III                                    | 531 (70.6)   | 165 (70.5)         | 366 (70.7)     |           |
| IV                                     | 144 (19.1)   | 42 (17.9)          | 102 (19.7)     |           |
| Pre-operative serum sodium (mmol/L, Mean ± SD) | 138.24 ± 3.64 | 138.41 ± 3.67 | 138.16 ± 3.63 | 0.28      |
| Pre-operative blood urea nitrogen (mg/dL, Mean ± SD) | 15.59 ± 9.66 | 16.55 ± 12.49 | 15.17 ± 8.16 | 0.30      |
| Pre-operative serum creatinine (mg/dL, Mean ± SD) | 0.90 ± 0.72 | 0.86 ± 0.43 | 0.92 ± 0.82 | 0.93      |
| Pre-operative serum albumin (g/dL, Mean ± SD) | 3.70 ± 0.68 | 3.71 ± 0.62 | 3.69 ± 0.71 | 0.91      |
| Pre-operative white blood cell count (x10E3/uL, Mean ± SD) | 8.09 ± 2.98 | 7.70 ± 2.70 | 8.27 ± 3.08 | 0.046     |
| Pre-operative international normalized ratio (INR, Mean ± SD) | 1.08 ± 0.25 | 1.06 ± 0.11 | 1.09 ± 0.29 | 0.98      |
| Pre-operative hematocrit (%) (Mean ± SD) | 37.49 ± 5.41 | 37.26 ± 5.25 | 37.6 ± 5.47 | 0.51      |

Analysis of 30-day post-operative outcome variables and length of hospital stay (Table 2) found a 38.2% complication rate ($n = 288$), a 13.7% reoperation rate ($n = 103$), a 14.9% readmission rate ($n = 71$), a 1.3% death rate ($n = 10$), and a mean length of stay of (12.75 ± 12.50) days. There were no significant differences between the group with concurrent neck dissection and the group without overall complications [206(35%) vs. 82(39.6%), $P = 0.23$], reoperations[70(13.5%) vs. 33(14.1%), $P = 0.81$], readmissions[46(13.7%) vs. 25(17.6%), $P = 0.27$], deaths [7(1.3%) vs. 3(1.3%), $P = 0.94$], and length of hospital stay[ (13.34 ± 13.71) days vs. 12.48 ± 11.94 days, $P = 0.99$].
Using the ACS-NSQIP database to examine the complication rates of total laryngectomy, our analysis demonstrated that concurrent neck dissection did not increase postoperative morbidity or mortality. The 30-day postoperative rate of complications, reoperation, readmission, and death was not significantly different between cases with or without neck dissection. Additionally, univariate regression did not demonstrate an effect of neck dissection on the rate of complications, reoperation, readmission, death or length of hospital stay. Furthermore, multivariate regression, which controls for the effect of each variable included in the analysis, reaffirmed that neck dissection was not associated with 30-day postoperative outcomes or length of stay.

| Variables               | All patients | No neck dissection | Neck dissection | P-value |
|-------------------------|--------------|--------------------|-----------------|---------|
| Complication [n (%)]    |              |                    |                 |         |
| No                      | 466 (61.8)   | 152 (65.0)         | 314 (60.4)      | 0.23    |
| Yes                     | 288 (38.2)   | 82 (35.0)          | 206 (39.6)      |         |
| Reoperation [n (%)]     |              |                    |                 |         |
| No                      | 651 (86.3)   | 201 (85.9)         | 450 (86.5)      | 0.81    |
| Yes                     | 103 (13.7)   | 33 (14.1)          | 70 (13.5)       |         |
| Readmission [n (%)]     |              |                    |                 |         |
| No                      | 407 (85.1)   | 117 (82.4)         | 290 (86.3)      | 0.27    |
| Yes                     | 71 (14.9)    | 25 (17.6)          | 46 (13.7)       |         |
| Death [n (%)]           |              |                    |                 |         |
| No                      | 744 (98.7)   | 231 (98.7)         | 513 (98.7)      | 0.94    |
| Yes                     | 10 (1.3)     | 3 (1.3)            | 7 (1.3)         |         |
| Length of total hospital stay (days, Mean ± SD) | 12.75 ± 12.50 | 13.34 ± 13.71 | 12.48 ± 11.94 | 0.99 |

Univariate analysis of the effect of concurrent neck dissection on 30 day outcomes (Table 3) and length of stay (Table 4) found that it was not predictive of complications [1.216(0.882–1.676), P = 0.23], reoperation [0.947(0.607–1.480), P = 0.81], readmission [0.742(0.436–1.264), P = 0.27], death [1.051(0.269–4.099), P = 0.94] or length of hospital stay [1.041(0.650–1.668), P = 0.87], readmission [0.822(0.461–1.466), P = 0.51], or length of hospital stay [0.975(0.471–2.47), P = 2.521].

As neck dissection is a fundamental tool in head and neck cancer management, studies have continued to explore its risks, with a special emphasis on its application in salvage laryngectomy. Aside from performance of ND for clinical or radiologically evident disease, in 1994, Weiss et al21 established that when the risk for positive neck lymph nodes exceeds 20% in a patient with a primary head and neck cancer and an N0 neck, ND is warranted. Some authors have applied this criteria to ND during salvage TL. The paper by Yao et al22 explicitly states, “Our philosophy is to perform elective neck dissections for a 20% or greater risk of occult metastases” in the setting of salvage laryngectomy. Amit et al16 reported that the rate of nodal metastasis in patients with recurrence who had clinically

### Table 3 Logistic regression of neck dissection on 30-day outcomes.

| Variables   | Univariate regression | Multivariate regression |
|-------------|-----------------------|-------------------------|
|             | OR P-value Lower Upper| OR P-value Lower Upper  |
| Complication | 1.216 0.23 0.882 1.676 | 1.360 0.31 0.750 2.452 |
| Reoperation  | 0.947 0.81 0.607 1.480 | 1.041 0.87 0.650 1.668 |
| Readmission | 0.742 0.27 0.436 1.264 | 0.822 0.51 0.461 1.466 |
| Death       | 1.051 0.94 0.269 4.099 |                          |

### Table 4 Linear regression of neck dissection on length of hospital stay.

| Variable   | Univariate Regression | Multivariate Regression |
|------------|-----------------------|-------------------------|
|            | Unstandardized B Beta | P-value 95%CI for B Lower Upper |
|            | Standardized Beta     |                         |
|            | Unstandardized B Beta | P-value 95%CI for B Lower Upper |
|            | Standardized Beta     |                         |
| Length of total hospital stay | -0.86 -0.03 0.38 -2.80 1.075 | -0.975 -0.042 0.58 -4.471 2.521 |
positive nodes at the time of their initial treatment was 50% thereby justifying neck dissection in these cases. In cases of recurrence in which patients had a N0 neck treated with radiation and comprehensive neck irradiation, Dagan et al found a low rate of occult neck disease (10%), and thereby found it justifiable to exclude neck dissection during salvage surgery, though only after restaging with contrast CT has shown no regional disease. At this time, predictors of neck disease in recurrent laryngeal cancer are being explored and will help head and neck surgeons better ascertain whether or not to pursue ND during salvage TL.

Our results concur with the previous findings of Schwartz et al, but the majority of current literature is focused on addressing whether ND is associated with a greater risk of complications with salvage TL in particular. Salvage TL itself is associated with a high rate of post-operative complications. Parsons et al reported a 20% incidence of pharyngocutaneous fistula after salvage surgery. In Dagan’s sample of patients with N0 necks and nodal irradiation at initial treatment, the authors found that patients who had ND during salvage surgery had a longer mean postoperative stay (15.1% ND vs 9.0% neck observed), higher rate of fistula (10% vs 3%), and greater rate of toxicities including wound complications, prolonged dependence of feeding tubes, aspiration pneumonia, and strictures (17% vs 12%); however, the statistical significance of these values was not addressed. In contrast, Yao et al reported no significant difference in operative mortality, average surgical time (4.8 h with and 4.2 h without ND, \( P = 0.11 \)) or rate of pharyngocutaneous fistula (12% with and 32% without ND, \( P = 0.06 \)). Presently, there is continued controversy whether concurrent neck dissection adds more risk of complications with salvage laryngectomy.

Similar to other registry studies, some limitations of our study deserve mentioning. A major limitation of this study was the inability to differentiate cases of TL with ND for primary cancer from those performed for recurrent cancer since ND during salvage surgery is of frequent debate. The ACS-NSQIP does not include tumor information, history of prior radiation, or history of chemotherapy making such a distinction impossible. Our findings that ND does not increase complication, reoperation, readmission rates, death, and length of stay may be influenced by the number of TLs performed for primary cancers in our sample which could outweigh salvage cases. Furthermore, there is no data in the literature reporting the current incidence of TL for primary cancer or salvage TL which prevents estimation of either cohort size. Additionally, there is no data in ACS-NSQIP on fistula formation, which addressed in most studies regarding ND and TL. Another limitation is that, given the increasing use of TL in salvage surgeries, which are associated with a high rate of complications, we would expect to see significantly more complications seen in our neck dissection group, as the proportion of salvage TLs increases; however, this was not seen in our data. Further analysis that is able to more specifically parse out the effects of salvage surgery is required. Another limitation of the NSQIP database is that there is no way to know why the concurrent neck dissections were done (therapeutic, elective, etc.) and different indications for neck dissections may predispose to varying complication rates. The authors believe, however, that the procedure is similar even when performed for different indications, which may minimize potential differences from this limitation. Finally, even with a large number of patients and use of a national database, this study is underpowered to show differences in outcomes of such low prevalence. Lastly, although the final model was well calibrated to the data, prospective studies with laryngectomy in relations to neck dissection specific metrics are needed to fully understand the scope of the postoperative outcomes. Nonetheless, the ACS-NSQIP provides a number of important advantages that shed light on the postoperative outcomes of laryngectomy in relations to neck dissection.

Strengths of this analysis include the use of a recent population. Our sample of cases from 2005 to 2012 is the most recent among the current literature. Such an up to date cohort represents the current trends in laryngeal cancer management. There is additional benefit to using a national database which allows for a large, multi-center cohort.

Future research should isolate cases of TL for primary from TL for salvage, then compare the rates of neck dissection to those without neck dissection. Use of a national database or other form of multicenter data would provide enough statistical power to determine significant differences in complication rates. The only other way to achieve significant power would be to use cases that may be dated in the 1990s, which in itself would limit application of the results to current laryngeal cancer management.

Conclusion

This is one of the first studies to analyze postoperative outcomes of laryngectomy with or without concurrent neck dissection using data aggregated across multiple institutions in ACS-NSQIP. Our study found that, in all total laryngectomies, there was no difference in length of hospital stay or in 30-day complication, reoperation, and readmission rates with or without concurrent neck dissection. Although the present study represents an initial attempt to identify postoperative outcomes of laryngectomy with or without concurrent neck dissection on a national level, the ACS-NSQIP database may not be sufficient to truly direct these initiatives. Further study in complications and outcomes of concurrent neck dissection in total laryngectomy is necessary with the changing trends in total laryngectomy as organ-preserving therapy increases in prevalence and more total laryngectomies are performed as salvage therapy.

Declaration of Competing Interest

None.

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