Predictors of Averse Events After Total Laryngectomy: An Analysis of the 2005-2011 NSQIP Datasets

Alexei Mlodinow1, Nima Khavanin1, Courtney Shires2, Sandeep Samant2, Jon Ver Halen3,*, John Kim1

1 Division of Plastic and Reconstructive Surgery, Northwestern University, Feinberg School of Medicine, Chicago, Illinois
2 Department of Otolaryngology- Head and Neck Surgery, University of Tennessee Health Science Center, Memphis, Tennessee
3 Division of Plastic and Reconstructive Surgery, Baptist Cancer Center, Memphis, Tennessee; Department of Surgery, St. Jude Childrens’ Research Hospital, Memphis, Tennessee; Department of Surgical Oncology, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee

Abstract

Background: We reviewed the 2005-2011 ACS-NSQIP database to evaluate factors associated with adverse events (AE) after total laryngectomy (TL).

Methods: All total laryngectomies performed from 2006 to 2011 were identified for analysis. The cohort was characterized with respect to preoperative and demographic characteristics, complications, reoperation, and mortality.

Results: 493 cases were identified. Complications of any category occurred in 189 cases (38.3%). Factors that were found to confer significant risk for medical complications were increased age [Odds Ratio (OR) 1.03], prior PCI (OR 2.84), disseminated cancer (OR 2.47), chronic steroid/immunosuppression use (OR 2.87), unintended weight loss > 10% over 6 months prior to surgery (OR 2.02), increasing work RVU total (OR 1.02), and increased anesthesia Z-score (OR 1.31). Only increased anesthesia Z-score (OR 1.27) was found to be a statistically significant risk factor for surgical complications. Chronic steroid/immunosuppression use (OR 3.16) and increased anesthesia Z-score (OR 1.29) were both found to be statistically significant risk factors of reoperation within 30 days.

Conclusions: NSQIP is the only dataset that correctly discerns between minimally invasive and wide excision in laryngectomy. The use of the NSQIP dataset may be imperfect, as pertinent details of chemotherapy and radiation, and procedure-specific complications, including fistula formation, are not tracked. In spite of this, our findings suggest avenues for improvement in the care of TL patients, and suggest directions for a laryngectomy-specific outcomes database.

Corresponding Author: Jon P Ver Halen, MD, FACS
Division of Plastic and Reconstructive Surgery, Baptist Cancer Center; Department of Surgery, St. Jude Childrens’ Research Hospital; Department of Surgical Oncology, Vanderbilt-Ingram Cancer Center
3268 Duke Circle, Germantown, TN 38139
Email: jpverhalen@gmail.com Tel: (206) 963-8714
Fax: (901) 227-9825

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Introduction

The care of patients with laryngeal cancer has changed dramatically in the last two decades. In 1991, the VA Laryngeal Cancer Study Group showed equivalent survival among patients undergoing laryngectomy versus chemoradiation. Subsequently, the use of primary chemoradiation in patients with advanced laryngeal cancer significantly increased, relative to the use of primary total laryngectomy. Total laryngectomy is now used more often as a salvage procedure after chemoradiation therapy. Salvage surgery has a lower rate of survival after the failure of organ preservation, and has a well-established increased rate of complications. In addition, the rate of postoperative fistula has increased from 52% to 84% over the past two decades. Wound healing complications and in-hospital death are significantly higher in patients undergoing pedicled or free-flap reconstruction, and in patients with advanced comorbidities. Prior radiation has also been found to be associated with increased rates of 30-day mortality.

The National Cancer Database (NCDB), Surveillance Epidemiology and End Results Medicare Database (SEER), Department of Veterans Affairs National Quality Improvement registry (VA NSQIP), Nationwide Inpatient Sample database, and single-institution databases have all been used to determine factors responsible for undesirable outcomes in laryngectomy patients. Our aim was to compare this data to that derived from the American College of Surgeons’ National Surgical Quality Improvement Program (ACS-NSQIP) database. The National Surgical Quality Improvement Program (NSQIP) was instituted by the American College of Surgeons (ACS) in 2004. Over 250 variables are collected and recorded by nurses trained in surgical and clinical review, and outcomes are tracked for 30 days following surgery. The participant use files provide a comprehensive set of reliable preoperative and intraoperative data, and postoperative data, with an only 1% rate of inter-observer disagreement.

We investigate the role of surgical complexity, preoperative radiation therapy, preoperative chemotherapy, and comorbidities in medical and surgical complications, as well as in the rate of reoperation in laryngectomy patients.

Methods

Sample Population

The ACS-NSQIP participant use files were reviewed for all total laryngectomies performed from 2006 to 2011, as represented by Current Procedural Terminology (CPT) codes 31360, 31365, 31390, and 31395 (Table 1). The cohort was characterized with respect to preoperative and demographic characteristics including age, BMI, gender, race, smoking status, alcohol use, diabetes, dyspnea, hypertension, dialysis, chronic steroid/immunosuppression use, radiotherapy within 90 days, chemotherapy within 30 days, and prior operation within 30 days. The cohort was then characterized with respect to overall complications, surgical complications (including surgical site infection,
dehiscence, and flap/graft/prosthesis failure), medical complications (including MI, pneumonia, reintubation, PE, ventilator use longer than 48 hours, renal insufficiency, renal failure, UTI, CVA, coma, neurologic deficit, cardiac arrest, bleeding, DVT, sepsis, septic shock, and death), and reoperation within 30 days. Detailed definitions of all variables tracked by NSQIP are available in the user guide.13

Statistical Analysis:

The population was split on the basis of presence of any complication. Those with and without complications were compared with respect to a variety of preoperative variables in order to identify associated factors. Independent sample t-tests and chi squared tests were used for continuous and categorical variables, respectively. A binomial logistic regression was then carried out to control for confounders and ascertain an independent odds ratio for each of the potential risk factors. Criteria for inclusion in the regression was p>0.2 and n>5 for all cells on initial screen. The same analysis was carried out for medical complications, surgical complications, and reoperation. Anesthesia time was changed into Z-scores representing standard deviation from the mean for the index CPT code.

Results

Sample Population

493 cases were abstracted from the participant use files on the basis of their CPT codes. Details of the cohort characteristics are represented in Table 2. The average age was 62.5 years (standard deviation of 11.4), and the average BMI 23.9 (standard deviation of 6.5). 384 of the patients (77.9%) were male, and 372 (75.5%) were white. 249 (50.5%) of patients were smokers, and 60 (12.2%) had significant alcohol consumption. Comorbidities present included diabetes (12.8%), dyspnea (28.6%), hypertension (46.25%), and dialysis (1.0%). Steroid use was present in 26 (5.3%) of patients, radiotherapy in 18 (3.7%), chemotherapy in 13 (2.6%), and prior operation in 48 (9.7%).

Complications of any category occurred in 189 cases (38.3%), with 72 cases (14.6%) experiencing surgical site complications, and 162 cases (32.9%) experiencing medical complications (Table 3). Specific surgical site complications included superficial incisional infections (6.3%), deep incisional infections (3.3%), organ space infections (1.2%), dehiscence (4.7%), and flap/graft/prosthesis failure (1.8%). Medical complications included MI (0.4%), pneumonia (5.1%), unplanned reintubation (3.0%), failure to wean from ventilator (4.3%), neurologic deficit (0.2%), cardiac arrest (1.4%), bleeding (21.1%), DVT (1.4%), sepsis

Table 1. List of included CPT codes

| CPT code | Description |
|---------|-------------|
| 31360   | Laryngectomy; total, without radical neck dissection |
| 31365   | Laryngectomy; total with radical neck dissection |
| 31390   | Pharyngolaryngectomy, with radical neck dissection; without reconstruction |
| 31395   | Pharyngolaryngectomy, with radical neck dissection; with reconstruction |
(4.9%), septic shock (0.4%), and death (2.0%). Reoperation within 30 days occurred in 67 cases (13.6%).

**Statistical Analysis**

11 potential risk factors fit inclusion criteria for the regression model for medical complications. Factors that were found to confer significant risk were increased age [Odds Ratio (OR) 1.03; 95% Confidence Interval (95% CI) 1.01-1.06], prior PCI (OR 2.84; 95% CI 1.30-6.20), disseminated cancer (OR 2.87; 95% CI 1.05-7.82), unintended weight loss (OR 2.02; 95% CI 1.10-3.70), increased RVU (OR 1.02, 95% CI 1.02-1.03), and increased anesthesia Z-score (OR 1.31, 95% CI 1.07-1.61). The results of the regression are represented in Table 4. 5 potential risk factors were included in the regression for surgical complications. Only increased anesthesia Z-score (OR 1.27, 95% CI 1.04-1.57) was found to be a statistically significant risk factor for surgical site complications. This is represented in Table 5. The regression model for reoperation included only 4 potential risk factors. Steroid use (OR 3.16; 95% CI 1.16-8.64) and increased anesthesia Z-score (OR 1.29; 95% CI 1.04-1.60) were both found to be statistically significant risk factors of reoperation within 30 days. This is represented in Table 6. All p values reached significance at less than 0.05.

**Discussion**

Although some surgical complications might be preventable, many are inherent risks associated with the procedure and are associated with safe management. Therefore, defining preventable or unnecessary adverse events is a challenge to ensure fair measurements of quality. Thirty-day adverse events, including complications, unplanned reoperation, and unplanned hospital readmissions represent a large financial burden to insurance payors, hospitals, and individual patients. In addition, they are increasingly surveyed as an indicator for health care quality, hospital performance, and a potential target for cost-containment.16 It has been estimated that approximately $15 billion is spent on the 17.6% of patients who are readmitted within 30
days of discharge, and this measure has been
identified by the Medicare Payment Advisory Commission (MPAC) as a major improvement item for covered

| Table 3. Patient adverse events, including overall complications, surgical complications, |
| Complication                          | Frequency (Total n=493) | n   | %   |
|---------------------------------------|-------------------------|-----|-----|
| Overall Complications                 |                         | 189 | 38.34% |
| Surgical Site Complications           |                         | 72  | 14.60% |
| Superficial Infection                 |                         | 31  | 6.29% |
| Deep Infection                        |                         | 16  | 3.25% |
| Organ Space Infection                 |                         | 6   | 1.22% |
| Dehiscence                            |                         | 23  | 4.67% |
| Flap/Graft Failure                    |                         | 9   | 1.83% |
| Medical Complications                 |                         | 162 | 32.86% |
| MI                                     |                         | 2   | 0.41% |
| Pneumonia                             |                         | 25  | 5.07% |
| Reintubation                          |                         | 15  | 3.04% |
| PE                                     |                         | 3   | 0.61% |
| Ventilator>48 Hours                    |                         | 21  | 4.26% |
| Renal Insufficiency                   |                         | 0   | 0.00% |
| Renal Failure                          |                         | 0   | 0.00% |
| UTI                                    |                         | 11  | 2.23% |
| CVA                                    |                         | 4   | 0.81% |
| Coma                                   |                         | 0   | 0.00% |
| Neurologic Deficit                    |                         | 1   | 0.20% |
| Cardiac Arrest                         |                         | 7   | 1.42% |
| Bleeding                               |                         | 104 | 21.10% |
| DVT                                    |                         | 7   | 1.42% |
| Sepsis                                 |                         | 24  | 4.87% |
| Septic Shock                           |                         | 2   | 0.41% |
| Death                                  |                         | 10  | 2.03% |
| Reoperation                            |                         | 67  | 13.59% |

| Table 4. Multivariable regression analysis for medical complications. |
| Risk Factor               | p Value | Odds Ratio | 95% Confidence Interval |
|---------------------------|---------|------------|-------------------------|
| Age*                     | 0.004   | 1.034      | 1.01 1.058              |
| BMI                       | 0.875   | 1.003      | 0.967 1.04              |
| COPD                      | 0.393   | 1.291      | 0.719 2.317             |
| Prior PCI*                | 0.009   | 2.837      | 1.298 6.199             |
| Hypertension              | 0.612   | 1.14       | 0.688 1.888             |
| Disseminated Cancer*      | 0.015   | 2.467      | 1.19 5.114              |
| Steroid Use*              | 0.04    | 2.866      | 1.051 7.815             |
| Weight Loss*              | 0.024   | 2.015      | 1.098 3.7               |
| ASA>2                     | 0.975   | 0.987      | 0.428 2.274             |
| Total RVU*                | < 0.001 | 1.024      | 1.016 1.031             |
| Anesthesia Time*          | 0.01    | 1.308      | 1.065 1.606             |

* indicates significant value (p < 0.05)

H-L Statistic: 0.612
c-Statistic: 0.809

| Table 5. Multivariable regression analysis for surgical complications. |
| Risk Factor               | p Value | Odds Ratio | 95% Confidence Interval |
|---------------------------|---------|------------|-------------------------|
| Diabetes                  | 0.429   | 1.378      | 0.622 3.055             |
| COPD                      | 0.094   | 0.487      | 0.209 1.132             |
| ASA>2                     | 0.393   | 1.607      | 0.542 4.768             |
| RVU                       | 0.122   | 1.005      | 0.999 1.012             |
| Anesthesia Time*          | 0.022   | 1.274      | 1.036 1.567             |

* indicates significant value (p < 0.05)

H-L Statistic: 0.598
c-Statistic: 0.69

identified by the Medicare Payment Advisory Commission (MPAC) as a major improvement item for covered
patients. The utility of these data extends to prevention measures: it could be used to assess risk factors for readmission, which in turn would allow the insurers to pool resources for those patients at greatest risk. However, this requires the ability to develop accurate methods to identify high-risk patients. The predictive power of currently available AE models is generally poor.

ACS-NSQIP is one of the largest, most comprehensive surgical databases available. In many regards, it has detail on preoperative and postoperative characteristics unparalleled by other resources. Given the broad base of patients captured, and the greater than 250 variables collected, it is uniquely positioned to examine specific issues in the laryngectomy cohort. Furthermore, NSQIP is the only multicenter, international, and validated database that specifically identifies the type of laryngectomy performed, and is thus the only database capable of correctly identifying total laryngectomy (as included in this study) versus partial or minimally invasive laryngectomy. In the most generic terms, tracking of adverse events after laryngectomy agrees with previously-published literature on the subject. However, we noted a number of significant, critical differences.

Compared to other databases, NSQIP greatly underestimates the utilization of laryngectomy. Using the National Cancer Database, Zhu, et al found 16,849 cases from 2003-2008, of whom 31% (approximately 5,100) underwent laryngectomy. Gourin, et al examined 78,478 cases between 1993 to 2008, and 24,856 cases between 2003 – 2008 using the Nationwide Inpatient Sample database. Schwartz, et al examined wound healing complications in 2063 patients undergoing total laryngectomy using the VA-NSQIP registry between 1989 – 1999. While current treatment strategies have led to a decrease in the utilization of total laryngectomy, this finding is likely because laryngectomy is not a specifically-tracked procedure within the NSQIP database, and could be addressed by adding it to the tracked procedures list.

ACS-NSQIP only identifies the use of chemotherapy and/or radiation therapy within the 30 and 90 days preceding the index procedure, respectively. Since a significant, and growing proportion of patients come to total laryngectomy after failure of primary treatment with chemotherapy and radiation, critical details of a given patient’s preoperative history are missed. For instance, our analysis showed no difference in 30-day outcomes regardless of the use of previous chemo- or radiation therapy. In fact, the identified cohort found only 18 patients (3.7%) who had a history of previous radiotherapy, and only 13 patients

Table 6. Multivariable regression analysis for reoperation.

| Risk Factor       | p Value | Odds Ratio | 95% Confidence Interval |
|-------------------|---------|------------|-------------------------|
| Steroid Use*      | 0.025   | 3.164      | 1.158 - 8.644           |
| ASA>2             | 0.32    | 1.859      | 0.548 - 6.306           |
| Total RVU         | 0.14    | 1.005      | 0.998 - 1.013           |
| Anesthesia Time*  | 0.023   | 1.286      | 1.035 - 1.598           |

* indicates significant value (p < 0.05)
(2.6%) who had a history of previous chemotherapy. Neither factors were found to be associated with adverse events. In the study by Zhu, et al, 42% of all patients had primary treatment with chemoradiation.\textsuperscript{17} Gourin et al found an increased rate of in-hospital death in patients with prior radiation (OR 3.94); Schwartz et al found an increased rate of wound complications after prior radiation (OR 1.63); finally, Ganly et al found increased rates of local wound (45% vs 25%) and fistula complications (32% vs 12%) after prior radiation therapy.\textsuperscript{4,6,7} Chemotherapy has been shown to increase adverse events in some studies.\textsuperscript{6} The South West Oncology Group reported a wound complication rate of 46% after 3 cycles of chemotherapy, whereas Cory et al reported a wound complication rate of 56% after induction chemotherapy.\textsuperscript{18} In Ganly’s study, multivariate analysis showed that primary combined chemotherapy and radiation was an independent predictor of local complications and pharyngocutaneous fistula after total laryngectomy.\textsuperscript{6}

Other risk factors for increased adverse events were generally in agreement with other studies. These included increased age, prior PCI, disseminated cancer, chronic steroid and/or immunosuppression use, unintended weight loss > 10% in the 6 months preceding the index procedure, increasing RVU total, and increased anesthesia time. Only increased anesthesia time was found to be a statistically significant risk factor for surgical site complications. Chronic steroid and/or immunosuppression use and increased anesthesia time were both found to be statistically significant risk factors of reoperation within 30 days. There were no preoperative characteristics specifically associated with 30-day mortality.

The sum of the relative value units (RVUs) was used to evaluate for the added complexity and risk of concurrent procedures, as has been described previously.\textsuperscript{19} RVUs reflect the relative level of time, skill, training and intensity required of a physician to provide a given service. RVUs therefore are a method for calculating the volume of work or effort expended by a physician in treating patients, and are set by CMS in association with a physician advisory council. For a patient undergoing multiple procedures, the respective RVU’s can be summed to estimate the total complexity of a given set of procedures (e.g., laryngectomy + free flap reconstruction + tracheostomy + feeding tube in a patient undergoing laryngectomy as one of multiple procedures). Given the heterogeneity of procedures identified in NSQIP, total work RVU is the best way to assess for the overall complexity of a given set of procedures performed on a patient in one setting. Previous studies have suggested that concomitant neck dissection and/or flap reconstruction with laryngectomy is associated with increased complications, although these findings are controversial.\textsuperscript{7,10-12} The use of RVU total, as in our study, is a much more appropriate measure of the overall magnitude of a given operation. Our findings further support the relationship between increasing surgical complexity with increased AE’s in patients undergoing TL.
There are a number of limitations to our study. The authors argue that while the number of cases is small compared to other database reviews, it is much larger than other studies of TL patients that have a similar level of granular detail with regard to demographic, operative and postoperative variables. Thus our findings are still relevant to the surgical community. In addition, the timeframe for tacking of preoperative radiation- and chemo-therapy is limited (as discussed above). Furthermore, NSQIP does not include data on total radiation dose, fractionation, exact radiation ports, and conventional radiation versus IMRT. Stratification into further categories based on these data points could result in further characterization of complications. There are several specific complications of laryngeal and neck operations that are not addressed in the NSQIP analysis. Success of voice rehabilitation, dysphagia, stricture, hypocalcaemia/hypoparathyroidism, hypothyroidism, chyle leak, shoulder weakness, lymphedema, and carotid rupture are examples. This system cannot address these specific issues at present, although modification of the standard NSQIP data acquisition protocol could be done to capture disease-specific information in the future. In addition, NSQIP does not include patient tumor characteristics. Initial TNM staging is not included, although “disseminated disease” represents M stage. The location of the primary tumor (larynx, hypopharynx, or oropharynx) is also not included. Finally, information on race/ethnicity, primary payer status, or level of education is not included in NSQIP. Other authors have shown that the decision of surgical versus nonsurgical therapy for laryngeal cancer was not related to comoridity, insurance status, or race/ethnicity. However, those with a higher level of education were more likely to undergo chemoradiation than laryngectomy.\textsuperscript{17} Regardless of these limitations, our study provides valuable insights into the treatment of patients undergoing TL.

Conclusions

Our analysis of total laryngectomies in the NSQIP database has a number of findings. Increased anesthesia time is the only factor significantly associated with all 3 categories of complications (medical complications, surgical complications, and reoperation). Overall, medical complications are much more common than surgical complications. Several factors were significantly related to medical complications, including age, prior PCI, disseminated cancer, steroid use, weight loss, total RVU, and prolonged anesthesia time. The use of the NSQIP dataset may be imperfect, as pertinent details of chemotherapy and radiation are not included. In spite of this, our findings provide data for improved patient care, and suggest directions for a laryngectomy-specific outcomes database.

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Conflicts of Interest:

The authors report no relevant financial disclosures related to this current work.
Ethical Approval:

De-identified patient information is freely available to all institutional members who comply with the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Data Use Agreement. The Data Use Agreement implements the protections afforded by the Health Insurance Portability and Accountability Act of 1996.

Disclaimer:

The NSQIP and the hospitals participating in the NSQIP are the source of the data used herein; they have not been verified and are not responsible for the statistical validity of the data analysis, or the conclusions derived by the authors of this study.

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