



Speech and swallowing outcomes after laryngectomy for the dysfunctional irradiated larynx

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Abstract

Purpose To characterize outcomes of total laryngectomy for the dysfunctional larynx after radiation.

Methods Retrospective case series of all subjects who underwent total laryngectomy for the irradiated dysfunctional larynx between 2000 and 2018 at an NCI-designated comprehensive cancer center at a single tertiary care academic medical center. Main outcomes included enteral tube feeding dependency, functional tracheoesophageal speech, and number and timing of postoperative pharyngeal dilations.

Results Median time from radiation to laryngectomy was 2.8 years (range 0.5–27 years). Functional outcomes were analyzed for the 32 patients with 1-year follow-up. Preoperatively, 81% required at least partial enteral tube feeding, as compared to 34% 1-year postoperatively ($p = 0.0003$). At 1 year, 81% had achieved functional tracheoesophageal speech, which was associated with cricopharyngeal myotomy ($p = 0.04$, HR 0.04, 95% CI 0.002–0.949). There were 34% of subjects who required at least one pharyngeal dilation for stricture by 1 year postoperatively. Over half (60%) of the cohort were dilated over the study period.

Conclusions Laryngectomy for the dysfunctional larynx improves speech and swallowing outcomes in many patients. Cricopharyngeal myotomy is associated with improved postoperative voice. While the need for enteral feeding is decreased, persistent postoperative swallowing dysfunction is common. Careful patient selection and education regarding functional expectations are paramount.

Keywords Head and neck oncology · Laryngectomy · Dysfunctional larynx · Radiation · Speech · Swallowing · Dysphagia · Tube feeding · Aspiration · Pharyngeal dilation · Cricopharyngeal myotomy

Introduction

Over the past two decades, radiation with or without chemotherapy has increasingly become a primary mode of treatment for patients with advanced laryngeal squamous cell cancer as part of organ preservation protocols. The landmark Veterans Administration (VA) trial [1] in 1991 followed by the Radiation Therapy Oncology Group (RTOG) 91–11 trial [2] in 2003 demonstrated similar survival rates comparing surgical and non-surgical arms or chemoradiation compared to radiation alone respectively. With the subsequent increase in nonsurgical primary treatment, the long-term sequelae of radiation are becoming more prevalent. Progressive and irreversible radiation-induced vascular damage and fibrosis engenders laryngopharyngeal dysfunction. This can result in

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tracheostomy dependence, recurrent aspiration pneumonia, impaired voice, and pharyngeal stricture [3]. Patterson et al. surveyed 42 patients 6 years after radiation and/or chemotherapy for head and neck cancer, of which 72% reported swallowing difficulties and 28% had chronic aspiration [4]. In a separate SEER-Medicare analysis, Xu et al. identified a 23.8% 5-year cumulative incidence of aspiration pneumonia, of which 84% were hospitalized and 45% required intensive care services [5].

There are limited options available to treat laryngopharyngeal dysfunction, or the “dysfunctional larynx”, after radiotherapy. A dysfunctional larynx for purposes of this report would include chronic laryngeal edema requiring tracheostomy, chronic aspiration or intractable dysphagia requiring feeding tube nutrition. Functional laryngectomy, which was first characterized for patients with intractable aspiration in the setting of neurogenic dysphagia [6, 7], is now an established option for the dysfunctional larynx. To date, speech and swallowing outcomes for this particular indication are not well described outside of three smaller case series [8–10]. Theunissen et al. performed a retrospective review that included 25 patients after a total laryngectomy for a dysfunctional larynx, from which they concluded that surgery had acceptable outcomes, but has significant major complications (45%) and mortality (8%) [8]. Hutcheson et al. then reviewed outcomes from 23 patients, for which there was decreased rates of pneumonia, nil per os status, and feeding tube status [10]. They also demonstrated a possible association between continued smoking after radiotherapy and a preoperative history of recurrent pneumonia with persistent tube feeding dependence. Most recently, Topf et al. reviewed outcomes from 19 patients and demonstrated a significant decrease in the need for gastrostomy tube dependence, but with persistent dysphagia [9].

Given the limited number of cases described and the few reliable predictors of functional outcomes among patients undergoing laryngectomy for the dysfunctional larynx, we sought to characterize outcomes for a larger cohort of subjects and to identify predictors of successful speech and swallowing.

Methods

A single institution retrospective case series was performed for all laryngectomy surgeries at an NCI-designated comprehensive cancer center between January 2000 and October 2018. Subjects who underwent laryngectomy for a dysfunctional larynx after radiotherapy with or without chemotherapy were included. All subjects were clinically without tumor recurrence at the time of laryngectomy. Patient demographics, clinical and tumor characteristics, surgical details, and postoperative outcomes are summarized in Table 1.

Table 1 Patient characteristics

	No. (%) of subjects
Sex	
Male	30 (70)
Female	13 (30)
Median (range) age at laryngectomy, years	62 (21–84)
Median (range) time between radiation and laryngectomy, years	2.8 (0.5–27)
Smoking status	
Never	4 (9)
Former	34 (79)
Current	4 (9)
Site of original tumor	
Larynx	31 (72)
Hypopharynx	5 (12)
Oral cavity/oropharynx	3 (7)
Unknown	4 (9)
T class of original tumor	
T1/T2	10 (23)
T3/T4	16 (37)
Unknown	17 (40)
Prior tumor treatment	
Radiation	43 (100)
Chemotherapy	28 (65)
Preoperative tracheostomy	31 (72)
Preoperative aspiration	31 (72)
Preoperative enteral feeding requirement	35 (81)

Characteristics of the 43 subjects who underwent total laryngectomy for a dysfunctional larynx

Postoperative outcomes included the need for enteral feeding, functional tracheoesophageal voice, aspiration events, the use of pharyngeal dilation, and the administration of botulinum toxin for cricopharyngeal dysfunction. Functional outcomes before and after laryngectomy were analyzed for subjects with at least 1 year of follow-up without recurrence of disease after surgery using Wilcoxon signed-rank tests. Bivariate analysis for variables listed in Table 2 was performed with Fishers exact tests, with inclusion of variables with $p < 0.10$ for subsequent regression analyses. Binomial logistic regression was performed to identify variables predicting speech and swallowing outcomes at 1 year postoperatively. All statistical tests were two-tailed and conducted in SPSS version 25 with $p < 0.05$ as a threshold for significance.

Results

Patient characteristics

A total of 43 subjects met inclusion criteria (Table 1). Subjects were predominantly male (70%) with a mean age of

Table 2 Bivariate testing of speech and swallowing outcomes

	No. (%) of subjects/median	Postoperative voice <i>p</i> values	Postoperative swallowing <i>p</i> values
Sex		0.63	1.00
Male	21 (66)		
Female	11 (34)		
Tobacco		1.00	0.44
Never	3 (9)		
Former	25 (78)		
Current	4 (13)		
Age at laryngectomy	61	1.00	1.00
Time between radiotherapy and laryngectomy	3	0.46	0.71
Original tumor site		0.42	0.34
Larynx	24 (75)		
Hypopharynx	4 (13)		
Oral cavity/oropharynx	2 (6)		
Unknown	2 (6)		
Original tumor T grade ^a		0.62	0.61
T1/T2	8 (25)		
T3/T4	14 (44)		
Unknown	10 (31)		
Chemotherapy		0.35	0.57
Administered	20 (63)		
Not administered	12 (37)		
Preoperative tracheostomy		0.30	0.47
Required	21 (66)		
Not required	11 (34)		
Preoperative need for at least partial enteral tube feeding		0.55	0.14
Required	26 (81)		
Not required	6 (19)		
Reconstructive type ^b		0.06	0.05
Primary closure	3 (9)		
Locoregional flap	5 (16)		
Free tissue transfer	24 (75)		
Cricopharyngeal myotomy at time of laryngectomy		0.06	0.08
Performed	28 (88)		
Not performed	4 (12)		
Tracheoesophageal puncture ^c		1.00	0.64
Primary	13 (41)		
Secondary	19 (59)		
Pharyngocutaneous fistula		1.00	0.25
Yes	10 (31)		
No	22 (69)		

Variables tested using Fisher exact tests for association with 1-year postoperative speech and swallowing outcomes

^aT grade defined as low grade (T1 and T2) versus high grade (T3 and T4)

^bReconstructive type defined as free tissue transfer, locoregional flap, or primary closure

^cTracheoesophageal puncture defined as at the time of laryngectomy or after the laryngectomy. Variables with *p* < 0.10 (bolded) were included for binomial logistic regression

61 years (range 21–84 years) at the time of laryngectomy. Median follow-up after the laryngectomy was 5.6 years (range 0.2–46 years). One-year follow-up data were available for 32 subjects (74%) at the time of this study. Median time from radiation to laryngectomy was 2.8 years (range 0.5–27 years). A total of 28 subjects (65%) also had a history of chemotherapy. The index tumor was laryngeal cancer in 31 patients (16 supraglottic, 6 glottic, 9 unknown subsite), hypopharyngeal cancer in five patients, oral cavity or oropharyngeal cancer in three patients, and an unknown primary site in four patients. There were 10 patients with T1 or T2 classifications for the initial tumor, 16 with T3 or T4 classification, and 17 with an unknown T classification. A total of 31 subjects (72%) had a tracheostomy prior to laryngectomy, 31 (72%) had aspiration based on aspiration pneumonias or documentation from a swallow study, and 35 (81%) required at least partial enteral tube feeding. Of the 43 subjects, 8 (19%) had one of the aforementioned laryngeal dysfunction types, 16 (37%) had at least two, and 19 (44%) had all three.

Reconstruction included free tissue transfer ($n = 31$, 72%), regional flaps ($n = 6$, 14%), or primary closure ($n = 6$, 14%). A total of 34 subjects (79%) underwent cricopharyngeal myotomy at the time of surgery. There were 17 (40%) and 23 (53%) subjects who underwent primary and secondary tracheoesophageal puncture, respectively. Three subjects were unable to undergo tracheoesophageal puncture. Complications included pharyngocutaneous fistulae ($n = 14$, 32%), 30 day readmission ($n = 10$, 24%), and a carotid blowout ($n = 1$) who died in hospice care 5 months after the laryngectomy. At 90 days, one other subject had died of an unknown cause. Two subjects had pathologic evidence of carcinoma in the elective laryngectomy specimen. One had microscopic disease with clear margins and was lost to follow up prior to a year, and therefore is not included in post-operative outcomes analysis. The other had positive margins and was treated with re-irradiation and thus was also not included in analyzing post-operative outcomes.

Functional outcomes: speech

At 1 year, 26 subjects (81%) had achieved functional tracheoesophageal speech. Of the six who had not achieved functional tracheoesophageal speech, at 3 years post-operatively two of the six had follow-up, and both had been successfully vocally rehabilitated at that time. On bivariate analysis (Table 2), no variables reached a statistically significant association with 1-year postoperative voice outcome. Based on a priori thresholds for logistic regression variable inclusion, cricopharyngeal myotomy and reconstructive types were selected as covariates. There was a

significant difference in the 1-year postoperative voice outcomes for subjects who underwent a cricopharyngeal myotomy at the time of laryngectomy ($p = 0.04$, HR 0.04, 95% CI 0.002–0.949). Multivariable logistic regression did not identify a statistically significant difference between free tissue transfer and locoregional flaps ($p = 0.09$) or primary closure ($p = 0.13$) for postoperative voice outcomes however.

Functional outcomes: swallowing

Functional outcomes were analyzed for the 32 patients with 1-year follow-up. Preoperatively, 26 subjects (81%) required at least partial enteral tube feeding, as compared to 10 subjects (31%) 1 year postoperatively (Fig. 1, $p = 0.0003$, Wilcoxon signed-rank test $Z = -4.0$). There were 11 subjects who required at least one pharyngeal dilation for stricture at 1 year. Two additional patients underwent botulinum toxin injection without pharyngeal dilation for pharyngeal spasticity by 1 year post-operatively, and an additional three patients had a combination of pharyngeal dilation and botulinum toxin over the 5 years reviewed. Overall, 60% of the cohort with at least 1-year follow-up was dilated over the study period (Fig. 2).

On bivariate analysis (Table 2), there was a statistically significant association between reconstructive type and 1-year postoperative swallowing status ($p = 0.05$), with free tissue transfer outperforming locoregional flaps. Cricopharyngeal myotomy was not statistically significant ($p = 0.08$), but was included along with reconstructive type as a covariate in logistic regression, based on a priori variable selection thresholds. Multivariable binomial logistic regression did not identify a statistically significant difference between free tissue transfer and locoregional flaps ($p = 0.08$) or primary closure ($p = 1.00$) for postoperative swallowing outcomes. There was no difference in cricopharyngeal myotomy in multivariate analysis ($p = 0.25$).

Discussion

Laryngopharyngeal dysfunction after radiation treatment for head and neck cancer can lead to severely diminished quality of life [3]. Functional laryngectomy is one of the few options for patients with intractable aspiration, debilitating dyspnea, and enteral tube feeding dependence. It is difficult to select and counsel patients for this procedure given the paucity of data regarding functional outcomes and their predictors. This study adds an additional 43 cases to the literature, for which 32 have 1-year postoperative functional data.

With regard to speech outcomes, most subjects in this study achieved functional tracheoesophageal speech at 1 year postoperatively, which is consistent with published

Fig. 1 Requirement of enteral tube feeding before and after laryngectomy. Percentages of subjects by reconstructive type requiring at least partial enteral tube feeding preoperatively and at 1 year postoperatively

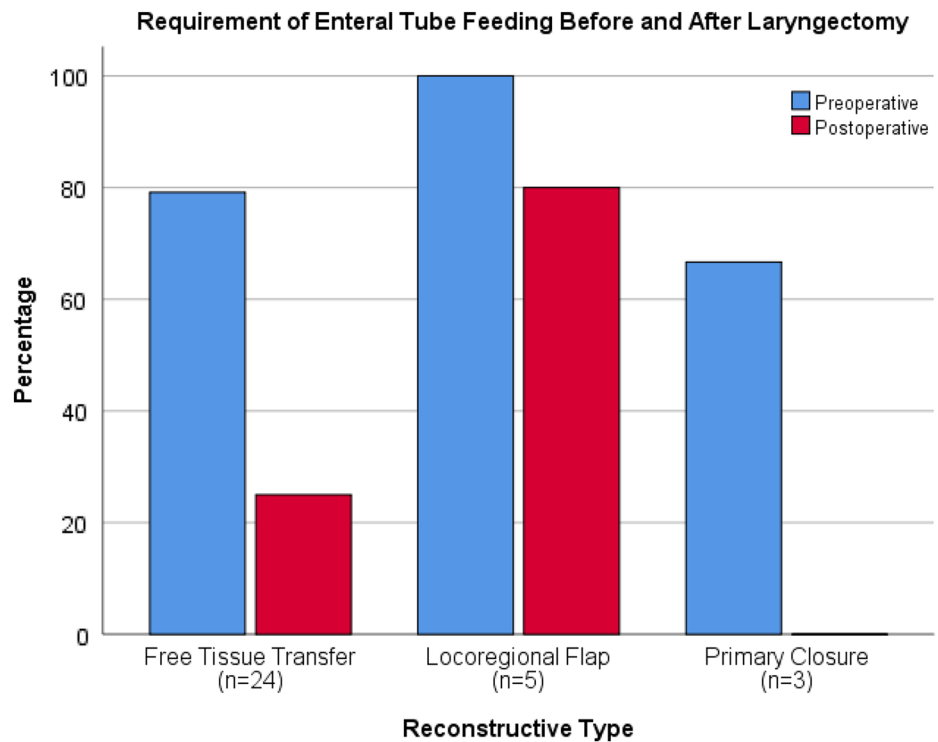
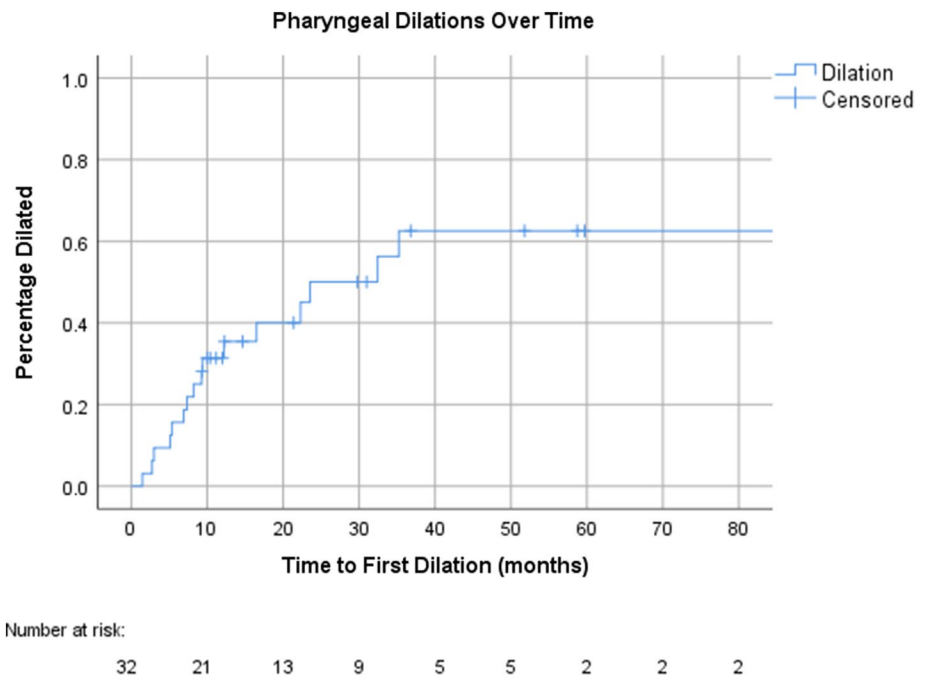


Fig. 2 Dilations over time. Time to event curve displaying the percentage of the cohort requiring pharyngeal dilation by months of follow-up. Patients were censored at the time to last follow-up or cancer recurrence



outcomes for all indications for laryngectomy [11]. Of those subjects who had not been vocally rehabilitated, those who were followed for 3 years post-operatively demonstrated significant rehabilitation at that point. Our study also confirms that cricopharyngeal myotomy is associated with improved voice outcomes postoperatively, as was initially postulated by Singer and Blom [12]. This has not yet been illustrated in

previous reports of laryngectomy for the dysfunctional larynx and represents one of the only identified predictors for successful postoperative speech. Of note, the present study did not demonstrate a significant difference in 1 year voice outcomes between primary and secondary tracheoesophageal punctures, the former of which has been advocated for earlier restoration of voice [11, 13].

Results from this study also provide surgeons and patients with additional information to establish realistic swallowing expectations after surgery. This study and previous case series [8–10] demonstrate that one-third of patients will likely not require enteral tube feeding 1 year postoperatively. Despite the substantial decrease of reliance on tube feeding, in our cohort, 60% of subjects still required pharyngeal dilation over the 5 years after surgery, and two additional subjects were treated with a single botulinum toxin injection within a year after surgery. This suggests a high prevalence of persistent swallowing dysfunction in this population. Previous work has shown that the presence of a feeding tube has a large negative impact on quality of life [14], so elimination of an enteral tube feeding requirement even with persistent dysphagia is still impactful for patients. Additionally, for those with continued pharyngeal stenosis, dilations can be safely done for many patients in the office or even at home [11].

Our results demonstrate similar outcomes between free tissue reconstruction and primary closure, with a trend towards worse outcomes with locoregional flaps. This affirms a recent multicenter review, which showed no significant difference between reconstruction with non-muscle vascularized tissue and primary closure for nutritional intake scores and understandability of speech [15]. Given the high rate of pharyngocutaneous fistulae in the salvage laryngectomy setting and the reported decrease in fistulae with microvascular reconstruction [15, 16], free tissue transfer will likely play a major role in reconstruction for the dysfunctional larynx. Future research in this setting could examine particular details of reconstructive technique and their relation to postoperative functional outcomes.

The promising outcomes of laryngectomy for the dysfunctional larynx are coupled with significant risk, as demonstrated in the literature and confirmed in our cohort. A systematic review and meta-analysis reported an overall complication rate after total laryngectomy of 67.5%, with the most common complications including pharyngocutaneous fistulae (28.9%), dysphagia (18.6%), pharyngeal stenosis or stricture (14.3%), and wound infection (14.1%), and with higher complication rates in the setting of preoperative radiation and/or chemotherapy [17]. The rate of pharyngocutaneous fistulae in our study was comparable to published ranges, especially considering that all subjects included in our study had preoperative radiation and/or chemotherapy. Importantly, two subjects died within 90 days of surgery, and morbidity has been similarly reported in other case series [8–10]. Thus, patients must be carefully counseled on the significant risks associated with a functional laryngectomy. There is likely a role for patient selection as well, given the high prevalence of comorbidities in this patient population and their associated surgical risks.

The main limitations of this study are its retrospective nature and small sample size. The median follow-up for the cohort was 5.6 years; however, only 32 subjects had one year postoperative data. Future analysis of this cohort may be better powered to identify predictors of successful functional outcomes. Quality of life and patient reported outcomes could also be incorporated into future studies, as these are critical to understanding patient perspectives of their own functional ability.

Conclusion

This study represents the largest case series of laryngectomy for the dysfunctional larynx. We confirm that the laryngectomy yields improved speech and swallowing outcomes in a majority of patients undergoing the procedure for post-radiation dysfunction. Cricopharyngeal myotomy was found to be associated with improved postoperative voice. Further study is warranted to determine if particular reconstructive techniques also yield better functional outcomes. While the need for enteral feeding is decreased regardless of technique, persistent postoperative swallowing dysfunction is prevalent. Additional research is needed to determine how we can better optimize functional outcomes. Although significant gains in quality of life can be achieved with a functional laryngectomy, the attendant risks of the procedure mandate careful patient selection and counseling.

Compliance with ethical standards

Ethical standards This study was performed in accordance with the ethical standards of the University of Michigan's Institutional Review Board (HUM00081554) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was deemed not applicable. There was no funding for this study, and the authors have no conflicts of interest to disclose.

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