ARTICLE IN PRESS

Am J Otolaryngol xxx (xxxx) xxx-xxx



Contents lists available at ScienceDirect

Am J Otolaryngol



journal homepage: www.elsevier.com/locate/amjoto

Shorter interval between radiation therapy and salvage laryngopharyngeal surgery increases complication rates following microvascular free tissue transfer

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ARTICLE INFO	A B S T R A C T	
A R T I C L E I N F O Keywords: Laryngectomy Radiation Salvage surgery Free flap Microvascular reconstruction Pharyngocutaneous fistula	<i>Purpose:</i> To evaluate how the interval between radiation and salvage surgery for advanced laryngeal cancer with free tissue transfer reconstruction influences complication rates. <i>Materials and methods:</i> This is a retrospective series of 26 patients who underwent salvage laryngectomy or laryngopharyngectomy with vascularized free tissue reconstruction (anterolateral thigh or radial forearm) following radiation or chemoradiation between 2012 and 2017 at a single academic center. The primary outcome was incidence of postoperative complications, including pharyngocutaneous fistula. Secondary outcomes included the need for a second procedure, time to resumption of oral feeding, feeding tube dependence, and hospital length of stay. <i>Results:</i> Salvage surgery was performed for persistence (7/26, 27%), recurrence/new primary (12/26, 46%), and dysfunctional larynges (7/26, 27%). Twenty-two (85%) defects were reconstructed with an anterolateral thigh free flap and 4/26 with a radial forearm free flap (15%). There were no flap failures. There were significantly more complications in patients undergoing surgery within 12 months of completion of radiation therapy (7/12, 58%) versus those undergoing surgery after 12 months (1/14, 7%; <i>p</i> = .02). Patients experiencing complications more often required a second procedure (4/7 vs. 0/1; <i>p</i> = .02), experienced a longer delay to initiation of oral diet (61 vs. 21 days; <i>p</i> = .04), and stayed in the hospital longer (28 vs. 9 days; <i>p</i> = .01). <i>Conclusions:</i> Shorter intervals between definitive radiation and salvage laryngopharyngeal surgery with free tissue reconstruction increases postoperative complications, hospital length of stay, and the likelihood of feeding tube dependence. Reconstructive surgeons can use these findings to help guide preoperative patient counseling and assess postoperative risk.	

1. Introduction

Organ-sparing primary radiation or combined chemoradiation therapy is commonly employed in the treatment of advanced laryngeal malignancy [1]. If salvage total laryngectomy or laryngopharyngectomy is needed for persistent or recurrent disease or dysfunctional larynges, the risk of wound complications, such as pharyngocutaneous fistula, is increased when operating in an irradiated surgical field [2–6]. Pharyngocutaneous fistulae after salvage laryngectomy or laryngopharyngectomy significantly increases the hospital cost, time to resumption of oral diet, feeding tube dependence for nutrition, and length of stay [7–9], all of which substantially impact patient quality of life during their initial recovery. Thus, it has long been the focus of efforts of reconstructive head and neck surgeons to innovate techniques for reducing these complications.

Despite the known higher rate of complications following salvage surgery and increased risk conferred by previous radiotherapy or chemoradiotherapy, there is a paucity of evidence addressing whether or not the actual interval between completion of organ-sparing therapy and performance of salvage surgery with reconstruction affects postoperative wound healing and reconstructive outcomes. A study by Sassler et al. in 1995 found that 10 of 13 (77%) patients requiring salvage surgery for head and neck squamous cell carcinoma of different sites experienced major wound complications if performed within 12 months of having completed combined chemoradiotherapy, versus only 1 of 5 (20%) experiencing complications if performed greater than

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https://doi.org/10.1016/j.amjoto.2018.06.009 Received 16 April 2018 0196-0709/ © 2018 Published by Elsevier Inc.

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12 months after treatment [6]. However, the specific site of cancer, type of surgery, and complications are not reported in the manuscript. More recently, Tsou et al. reported a markedly higher pharyngocutaneous fistula rate in those undergoing salvage laryngopharyngectomy within 3 months of combined chemoradiotherapy (26/35, 74%) versus those undergoing surgery > 3 months from completion of therapy (2/13, 15%) [3]. However, this series included patients who mostly underwent primary closure (31/48, 65%), and did not report how the time interval to surgery affected the complication rate in patients who underwent free tissue transfer reconstruction.

To our knowledge, a study that specifically addresses the complication rate with regards to the interval between radiation and surgery in salvage laryngectomy or laryngopharyngectomy patients reconstructed with vascularized free tissue does not exist. Thus, the purpose of the present study was to investigate whether or not a shorter interval between radiation and salvage surgery affects free tissue transfer reconstruction outcomes in a population of patients with advanced laryngeal cancer. We hypothesized that there would be a higher incidence of postoperative complications in those undergoing salvage procedures sooner after completion of organ-sparing treatment.

2. Methods

The following study was deemed exempt by the Institutional Review Board at the lead author's institution. A retrospective review of all salvage total laryngectomy or laryngopharyngectomy cases performed between January 2012 and January 2017 was conducted at the University of California - San Francisco, a tertiary care academic referral center for head and neck oncologic surgery. Eligible cases included patients who were treated with prior radiation therapy or concurrent chemoradiation with subsequent persistence, recurrence, or a dysfunctional larynx leading to a total laryngectomy or laryngopharvnectomy. Through a comprehensive chart review, we collected demographic, historical, and clinical data, including medical comorbidities, initial tumor staging, and surgical indications prior to surgical intervention as well as surgical characteristics (type of surgery and reconstruction, whether or not a neck dissection was performed, length of hospital stay) and post-surgical outcomes, including complications, need for additional procedure or readmission, and time to oral feeding (Table 1).

The principal variable of interest was the interval between the completion date of radiation or combined chemoradiation therapy and the date of salvage laryngeal surgery. The primary outcome was the incidence postoperative complications, in particular, the development of pharyngocutaneous fistula(e). Secondary outcomes we assessed included the time to oral feeding, hospital length of stay, and the need for additional procedures for treatment of complications. Follow-up with the reconstructive surgeon continued through the immediate postoperative period, until resumption of oral diet or resolution of complications. It is important to note that at our institution, the standard is to place salivary bypass tubes in the operating room after salvage procedures following free flap reconstruction and to maintain a strictly non-oral diet for 2 weeks.

The study population was divided into the two following cohorts according to the interval between prior radiation and salvage surgery: a "short" interval group who underwent surgery within 12 months of radiation completion and a "long" interval group who underwent surgery at an interval > 12 months from completion of radiation. Subset analyses were then conducted to assess the influence of treatment interval on the incidence of complications. Descriptive statistics, including counts, means, and standard deviations were performed in Excel V.14 (Microsoft, Redmond, WA, USA). Two-tailed *t*-tests were employed to test for significant differences in continuous variables, while Chi-square tests were used to test for differences in categorical or dichotomous variables. Significance was assigned for *p*-values < 0.05. We performed a univariate analysis of potential influential variable for

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Table 1

Clinical characteristics of salvage laryngectomy/laryngopharyngectomy patients, entire cohort (n = 26).

Characteristic	No. or avg.	Percent or SD	
Age	62.1 years	10.1 years	
Gender (male)	19	73%	
Comorbidities			
Hypothyroidism	6	21%	
Smoker (> 10 pack year)	18	69%	
Alcohol use	8	31%	
BMI. kg/m^2	24.1	5.2	
ASA class			
2	5	19%	
3	21	81%	
Initial clinical stage			
2	5	19%	
3	11	42%	
4	5	19%	
Prior treatment			
Chemoradiotherapy	18	69%	
Radiotherapy alone	8	31%	
Reason for surgery			
Persistence	7	27%	
Recurrence/new primary	12	46%	
Dysfunctional larynx	7	27%	
Surgery			
Laryngectomy	16	62%	
Laryngopharyngectomy	10	38%	
Neck dissection	17	65%	
Interval to surgery after prior treatment (months)	35.9	64	
Surgery within 12 months	12	46%	
Type of reconstruction			
Anterolateral thigh	22	85%	
Radial forearm	4	15%	
Average length of stay, days	15	18	
Complications			
Major ^a	4	15%	
Minor ^b	7	27%	
Total pharyngocutaneous fistulae	7	27%	
Average time to P.O., days	30	24	

^a Major complications were those that required an additional surgical procedure for management (e.g., pharyngocutaneous fistula that required re-operation for additional reconstruction).

^b Minor complications include those that resolved with conservative treatment such as further NPO time, local wound care, and prolonged salivary bypass tube use. Note that this includes pharyngocutaneous fistulae that resolved without need for intervention.

the development of complications but were unable to perform a multivariate analysis given the limited sample size.

3. Results

3.1. Patient characteristics

Twenty-six patients underwent salvage laryngectomy or laryngopharyngectomy during the study period. Table 1 shows the demographic and clinicopathologic characteristics of the entire study cohort. The majority had received combined chemoradiotherapy (69%). Approximately two-thirds (16/26) underwent salvage laryngectomy while 10 underwent laryngopharyngectomy. The majority of patients also underwent a concomitant neck dissection (65%). Reconstruction was performed with an anterolateral thigh free tissue transfer in 22 (85%); the remaining were reconstructed with a radial forearm free flap. The average time interval to surgery after having completed organ-sparing therapy was 35.9 months (SD = 64.4 months). There were no partial or complete flap failures. There were no flap takebacks. Twelve (46%) underwent ablative surgery and reconstruction within 12 months. Overall, 8 patients experienced 11 complications, including 4 major complications (defined as those needing a Download English Version:

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