

PREVENTION OF WOUND COMPLICATIONS FOLLOWING SALVAGE LARYNGECTOMY USING FREE VASCULARIZED TISSUE

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Abstract: *Background.* Total laryngectomy following radiation therapy or concurrent chemoradiation therapy is associated with unacceptably high complication rates because of wound healing difficulties. With an ever increasing reliance on organ preservation protocols as primary treatment for advanced laryngeal cancer, the surgeon must develop techniques to minimize postoperative complications in salvage laryngectomy surgery. We have developed an approach using free tissue transfer in an effort to improve tissue vascularity, reinforce the pharyngeal suture line, and minimize complications in this difficult patient population. The purpose of this study was to outline our technique and determine the effectiveness of this new approach.

Methods. We conducted a retrospective review of a prospective cohort and compared it with a historical group (surgical patients of Radiation Therapy Oncology Group (RTOG)-91-11 trial). Eligibility criteria for this study included patients undergoing salvage total laryngectomy following failed attempts at organ preservation with either high-dose radiotherapy or concurrent chemo/radiation therapy regimen. Patients were excluded if the surgical defect required a skin paddle for pharyngeal closure. The prospective cohort consisted of 14 consecutive patients (10 males, 4 females; mean age, 58 years) who under-

went free tissue reinforcement of the pharyngeal suture line following total laryngectomy. The historical comparison group consisted of 27 patients in the concomitant chemoradiotherapy arm of the RTOG-91-11 trial who met the same eligibility criteria (26 males, 1 female; mean age, 57 years) but did not undergo free tissue transfer or other form of suture line reinforcement. Minimum follow-up in both groups was 12 months.

Results. The overall pharyngocutaneous fistula rate was similar between groups—4/14 (29%) in the flap group, compared with 8/27 (30%) in the RTOG-91-11 group. There were no major wound complications in the flap group, compared with 4 (4/27, 14.8%) in the RTOG-91-11 group. There were no major fistulas in the flap group, compared with 3/27 (11.1%) in the RTOG-91-11 group. The rate of pharyngeal stricture requiring dilation was 6/14 (42%) in the flap group, compared with 7/27 (25.9%) in the RTOG-91-11 group. In our patients, the rate of tracheoesophageal speech was 14/14 (100%), and complete oral intake was achieved in 13/14 (93%) patients. Voice-Related Quality of Life Measure (V-RQOL) and Performance Status Scale for Head and Neck Cancer Patients (PSS-HN) scores suggest that speech and swallowing functions are reasonable following free flap reinforcement.

Conclusions. Free vascularized tissue reinforcement of primary pharyngeal closure in salvage laryngectomy following failed organ preservation is effective in preventing major wound complications but did not reduce the overall fistula rate. Fistulas that developed following this technique were relatively small, did not result in exposed major vessels, and were effectively treated with outpatient wound care rather than readmission to the hospi-

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tal or return to operating room. Speech and swallowing results following this technique were comparable to those following total laryngectomy alone. ©2007 Wiley Periodicals, Inc. *Head Neck* 29: 425–430, 2007

Keywords: laryngectomy; fistula; wound complications; radiation; chemotherapy; flap

Salvage surgery after intensive combined chemoradiation treatment is associated with high complication rates because of wound healing problems. Pharyngocutaneous fistula is one of the most common wound healing complications following laryngectomy. Numerous risk factors, including radiotherapy,^{1–4} nutrition, postoperative hemoglobin,^{1,3} diabetes,¹ liver disease,¹ and stage,⁵ for fistula development have been identified in various retrospective studies. With the advent of organ preservation therapy for advanced head and neck cancer, the use of combined chemotherapy and radiation therapy has become increasingly frequent. A recent prospective randomized trial supports the role of combined chemoradiotherapy for treatment of advanced laryngeal cancer.⁶ However, salvage laryngectomy in a setting of previous chemoradiotherapy is associated with high rates of wound complications, ranging from 59%⁷ to 77%.⁸ The toxic effects of radiation in conjunction with chemotherapeutic agents on normal tissues are well established.^{9,10} Microscopically, these effects are manifested by obliterative endarteritis and fibrosis.¹¹ Therefore, methods to improve tissue vascularity and healing should increase surgical success rates. Since November 1999, we have used free vascularized tissue to reinforce pharyngeal closures (pharyngeal interposition graft [PIG]) in salvage laryngectomy patients in a setting of previous chemoradiation. The purpose of this study was to determine whether PIG affects the incidence of wound complications in salvage laryngectomy patients following organ preservation therapy for advanced laryngeal carcinoma.

PATIENTS AND METHODS

Design. This was a retrospective review of a prospective cohort (PIG group) and comparison with a historical group (surgical patients in arm 2 of Radiation Therapy Oncology Group (RTOG)-91-11).

Patients. We compared 2 groups of patients—a prospective cohort (PIG Group) and a cohort of historical controls (RTOG-91-11 Group). Data for the PIG group were obtained from medical

Table 1. Patient characteristics.

Patient demographics	PIG group	RTOG 91-11 group
Mean age, y	57.8 (40–73)	57.0 (40–70)
Sex, M:F	10:4	26:1
Stage		
I	1 (7)	0
II	0 (0)	0
III	6 (43)	21 (77.8)
IV	7 (50)	6 (22.2)
Initial treatment		
Chemoradiation	12 (86)	27 (100)
Radiotherapy	2 (14)	0
Time interval from initial treatment	24 months (range, 7–90)	n.a.
Postoperative follow-up	30 months (range, 12–53)	41 months (range, 11–98)
Current status		
NED	11 (79)	19/27 (70)
DOD	0 (0)	n.a.
AWD	3 (21)	n.a.

Abbreviations: PIG, pharyngeal interposition graft; NED, no evidence of disease; DOD, died of disease; AWD, alive with disease.

*Values in parentheses are percentages unless indicated otherwise.

records. Data for the RTOG-91-11 group were previously published and used with permission for the purpose of comparison. Patient data for both groups are summarized in Table 1. All patients had a minimum follow-up of 12 months.

Pharyngeal Interposition Graft Group. Patients included in the study were those who were at high risk for wound complications following total laryngectomy. This study population included patients with recurrent laryngeal carcinoma requiring salvage total laryngectomy who were previously treated with combined chemotherapy and radiotherapy and patients with treatment-related tissue damage (eg, chondroradionecrosis) severe enough to warrant total laryngectomy in the absence of cancer. Patients were excluded if the surgical defect required a skin paddle for pharyngeal closure (ie, laryngopharyngectomy defects).

From September 1999 to February 2003, 18 consecutive patients underwent salvage laryngectomy following previous organ preservation therapy for advanced laryngeal carcinoma. All patients were treated surgically at the University of Michigan Health Center. Staff members in the Division of Head and Neck Surgery performed all salvage surgery and microvascular free tissue transfers. Minimum follow-up was 12 months, and mean follow-up was 30 months. Primary treatment consisted of concomitant platinum-based chemotherapy and radiotherapy in 12/14 (86%) patients, and

primary high-dose radiotherapy in 2/14 (14%) patients. A chemoradiation regimen was delivered as part of an induction and concurrent chemotherapy and radiation therapy protocol at the University of Michigan Medical Center in 7/14 (50%) of patients. Indications for surgical salvage included recurrence in 12/14 (86%) patients and chondronecrosis in 2/14 (14%) patients.

Surgical Technique. Surgical salvage consisted of total laryngectomy. Bilateral neck dissection was performed on patients with recurrent tumor. All patients received primary tracheoesophageal puncture. All pharyngeal defects were closed primarily in a multilayered T configuration. Patients were excluded if the defect required a skin paddle for pharyngeal closure (ie, laryngopharyngectomy defects). Fascial free tissue transfer was performed to reinforce the primary pharyngeal closure in all patients. The flap was held in position with tacking sutures to prevertebral fascia on both sides of the pharynx. The skin paddle was left on the PIG if the native suprastomal neck skin appeared nonviable after elevation.⁶ Reconstructive data are summarized in Table 2. Patients were started on an oral diet and the speech prosthesis was inserted on postoperative day 28.

RTOG-91-11 Group. From 1992 to 2000, 27 patients who underwent salvage laryngectomy with primary pharyngeal closure without vascularized tissue reinforcement were enrolled in the concomitant chemotherapy and radiotherapy arm of the RTOG Trial 91-11. All patients initially received concomitant chemotherapy consisting of cisplatin (100 mg/m²) on days 1, 22, and 43 of radiotherapy (RT), and RT consisting of 70 Gy total dose in 2 Gy fractions delivered over 7 weeks. This group also included 2 patients with chondronecrosis of the larynx or laryngeal dysfunction, similar to our flap group demographics.

adionecrosis of the larynx or laryngeal dysfunction, similar to our flap group demographics.

Variables under Study. A wound complication was defined as any deviation from the expected healing process. Wound complications were classified as major or minor, as defined by Weber et al.⁷ A major complication was defined as one that leads to rehospitalization or death. A minor complication was defined as one that is self-limited, managed with outpatient care, and does not require hospitalization.

The secondary outcome variables were speech and swallowing functions using validated quality of life (QOL) instruments (Voice-Related Quality of Life Measure, V-RQOL,¹² and Performance Status Scale for Head and Neck Cancer Patients, PSS-HN¹³) and nutritional mode. Data were also collected on presence of fluent tracheoesophageal puncture (TEP) speech, time to oral intake, flap complications, and donor site complications.

The V-RQOL is a 10-item self-administered validated voice outcomes measure. Scores are reported in 2 domains: social-emotional and physical functioning, and a total score. Two data sets were used for comparison. The first consisted of normative data from a published validation study on a population of 21 facial cosmetic patients without a known voice disorder.¹² The second consisted of a cohort of 12 patients who underwent total laryngectomy without PIG. These normative data were compared with V-RQOL scores obtained from the PIG group. The instrument scores on a scale from 0 to 100, and a higher score indicated better function.

The Performance Status Scale is a 3-item observer-rated validated speech and swallowing outcomes measure.¹³ The 3 items include eating in public (scale of 1–6), normalcy of diet (scale of 1–10), and understandability of speech (scale of 1–5), where a higher score indicates better function.

Nutritional mode (categorical variable) was assessed, and patients were assigned to one of the following categories: (1) nothing by mouth, (2) tube feeds, trial oral intake, (3) combined oral and tube feeds, (4) nutritional supplements only taken by mouth, (5) oral intake with nutritional supplements, and (6) oral intake alone without supplements.

Statistical Analysis. Comparisons of fistula rate between the PIG group and the RTOG-91-11 group were made using a 2-tailed Fisher's exact

Table 2. Reconstructive data.

	No. (%)
Donor site	
Radial forearm	9/14 (64)*
Anterolateral thigh	4 (29)
Lateral arm	1 (7)
Mean surface area, cm ²	101.3
Tissue components	
Fascial	9 (64)
Fasciocutaneous	5 (36)
Flap death	0
Donor site complications	
Radial forearm—wound breakdown	2 (11.1)

*Values in parentheses are percentages.

test. V-RQOL scores from the normal cohort as well as standard laryngectomy group (without PIG) were compared with V-RQOL scores in the PIG group using a student's 2-tailed *t* test. A 2-tailed *p* value of .05 or less was considered to be statistically significant.

Approval was obtained from the University of Michigan Institutional Review Board (IRB Approval no. 2002-0459).

RESULTS

Wound Complications. Table 3 summarizes the wound complications. Overall, pharyngocutaneous fistulas occurred in 4/14 (29%) patients in the free flap group and 8/27 (30%) patients in the RTOG-91-11 group. There were 3 major fistulas (requiring hospitalization, reoperation, or resulting in death) in the RTOG-91-11 group, compared with 0 in the PIG group, but this was not statistically significant ($p = .264$). The rate of major wound complications was higher in the RTOG-91-11 group (14.8%), compared with that in the PIG group (0%), but was not statistically significant ($p = .173$).

Speech and Swallowing Functions. V-RQOL scores were obtained in 13/14 (93%) patients. One patient was excluded who had a stomal recurrence prior to survey administration. The patients with a PIG had a total score of 66.5, whereas patients

who had a total laryngectomy without a PIG had a total score of 65.8. This difference was not clinically significant, which suggests that a PIG is neither an advantage nor a disadvantage in terms of voice-related QOL. The control group of "normal" patients had a total score of 98.0, which, as expected, was statistically significant ($p < .001$). Subscales and scores are shown in Table 4.

All 14 patients were alive and were communicating fluently with a tracheoesophageal voice prosthesis.

Performance Status Scale scores were obtained in all patients. All patients supported their nutritional needs exclusively with oral intake. The mean time to oral intake was 40 days. With respect to nutritional mode, 9/14 (64%) patients were eating *per orum* with no need for oral supplements, 4/14 (29%) patients were eating *per orum* but also required oral supplements, and 1/14 (7%) patients required enteric supplementation.

DISCUSSION

This study suggests that, although PIG did not alter the pharyngocutaneous fistula rate, major wound complications were reduced. Wound complications in patients undergoing PIG were effectively treated with outpatient wound care rather than major salvage flap procedures in the operating room. This result suggests that free vascularized tissue reinforcement of primary pharyngeal closure in this patient population may be beneficial in preventing surgical intervention for pharyngocutaneous fistula. In other words, PIG may "convert" major wound complications to minor wound complications. This finding, if further substantiated by prospective data, would be clinically important because of decreased patient morbidity and mortality and savings to the health-care system. Moreover, given the high rates of tracheoesophageal speech and complete oral intake, PIG does not seem to adversely affect speech and swallowing.

Patients who may benefit from PIG are those at high risk for wound complications. These include, but are not limited to, the following: (1) patients with recurrent laryngeal carcinoma requiring salvage total laryngectomy who were previously treated with combined chemotherapy and radiotherapy, and (2) patients with treatment-related tissue damage (eg, chondroradionecrosis) severe enough to warrant total laryngectomy in the absence of cancer. A similar paper has shown that free tissue reconstruction of the

Table 3. Wound complications.

	PIG group	RTOG 91-11 group
Major complications		
Pharyngocutaneous fistula	0	3 (11.1%)
Wound infection	1 (5.6%)	1 (3.7%)
Death	0	0
Minor complications		
Wound dehiscence/infection	2 (11.1%)	9 (33.3%)
Pharyngocutaneous fistula	5 (27.8%)	5 (18.5%)
Mean number per patient	1.6 (1-3)	n.a.
Mean duration per patient (days)	42 (13-134)*	n.a.
Pharyngeal stenosis requiring dilation		
Total number	6 (33.3%)	7 (25.9%)
Mean number of dilations per patient	3 (1-10)	n.a.

Abbreviations: PIG, pharyngeal interposition graft; RTOG, Radiation Therapy Oncology Group.

Major complication—one that leads to rehospitalization or death. Minor complication—one that is self-limited, managed with outpatient care, and does not require hospitalization.

*The patient listed as having a fistula for 134 days actually had an intermittent fistula, draining occasionally prior to healing.

Table 4. Voice-Related Quality of Life (V-RQOL) scores.

Group	Social-emotional	Physical functioning	Total
Laryngectomy with PIG (<i>n</i> = 14)	63.5 ± 20.8	71.2 ± 21.1	66.5 ± 20.3
Laryngectomy without PIG (<i>n</i> = 12)	68.2 ± 29.0	64.2 ± 26.4	65.8 ± 26.2
Normal population* (<i>n</i> = 21)	98.8 ± 4.2	97.3 ± 5.8	98.0 ± 3.9

Abbreviation: PIG, pharyngeal interposition graft.

All scores are mean ± SD.

**p* < .001.

hypopharynx following chemoradiation results in lower rates of wound complications.¹⁴ In total laryngectomy patients, wherein primary pharyngeal closure is possible, the pectoralis major myofascial flap has been shown to result in a pharyngocutaneous fistula rate of less than 1%.¹⁵ In this retrospective study, however, only 26% of patients had a history of prior radiation, and it is not known whether any patients had previous chemoradiotherapy. Nevertheless, the positive impact on wound healing should be achieved by bringing unirradiated tissue with good blood supply, from any source, regional or distant. Our rationale for using free tissue transfer is related to the following factors: (1) pectoralis myofascial flaps result in significant additional shoulder morbidity, particularly in patients undergoing ipsilateral neck dissection; (2) the pectoralis muscle may impair postoperative speech fluency because of alteration of the shape of the tracheostoma; and (3) the bulk of the pectoralis flap often makes it difficult to close the skin incision in a tension-free manner, making suprastomal skin necrosis more likely.

Preoperative radiotherapy has been identified in several studies as a significant risk factor for the development of pharyngocutaneous fistula following laryngectomy.^{1,3,4} Other studies examine heterogeneous populations undergoing a variety of surgeries, including surgery for the primary tumor (ie, laryngectomy, laryngopharyngectomy, composite resection) and surgery for nodal disease (ie, neck dissection).^{16,17} Chemoradiation in these studies has been found to be associated with high complication rates (35–38%) but cannot be extrapolated to a uniform population. We sought to clearly define the utility of vascularized tissue in patients with a specific defect in a high-risk patient population. The quality of a study such as this one would be improved by introducing a comparison group with primary closure alone and evaluating the effect of a pharyngeal bypass tube.

Although speech results in the study population were found to be inferior to normative data from normal control patients, they were no differ-

ent from data obtained from patients who underwent standard laryngectomy (without PIG). Furthermore, the overwhelming majority of patients were communicating fluently with a tracheoesophageal voice prosthesis. It is important to know that the PIG, which is an additional fascial layer over the pharyngeal closure, does not impede with the vibratory (pharyngoesophageal) segment. Moreover, the rate of pharyngeal stenosis requiring dilation is not higher, and postoperative swallowing function is satisfactory in the study population, suggesting that the addition of this fascial layer also does not adversely affect swallowing function.

CONCLUSIONS

Free vascularized tissue reinforcement of primary pharyngeal closure in salvage laryngectomy following chemoradiation is an effective technique to prevent major wound complications, although it does not alter the overall fistula rate. Patients who develop a pharyngocutaneous fistula after a PIG procedure tend to have relatively small fistulas without great vessel exposure and can be effectively treated with outpatient wound care rather than hospital readmission and imminent return to the operating room. In other words, PIG may “convert” major wound complications into minor wound complications, thereby decreasing morbidity, mortality, and cost. Speech and swallowing results following this technique are comparable to those following total laryngectomy alone. The complexity and added cost of such surgery emphasizes the need to carefully identify those patients likely to benefit from primary chemoradiation in order to minimize the number of patients requiring salvage surgery.

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