The Role of Pectoralis Major Muscle Flap in Salvage Total Laryngectomy

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Objective: To assess the utility of the pectoralis major muscle flap (PMMF) in patients undergoing salvage total laryngectomy.

Design: Retrospective cohort analysis.

Setting: Tertiary care cancer center.

Patients: The study included 461 patients who underwent laryngectomy. Eighty of them underwent salvage surgery with primary pharyngeal closure.

Interventions: Of the 80 patients, 69 (86%) underwent primary pharyngeal closure alone and 11 (14%) underwent a PMMF, which was used to buttress the pharyngeal suture line.

Main Outcome Measure: Two hundred thirty-six variables were recorded for each patient. Complications related to pharyngeal closure were measured.

Results: Sixty-four percent of the patients who underwent PMMF also underwent chemoradiation therapy as the initial definitive treatment compared with 25% in the non-PMMF group (P = .03). On multivariate analysis, chemoradiation therapy was the only independent predictor of pharyngocutaneous fistula formation (relative risk, 1.82; P = .02). Nevertheless, the pharyngocutaneous fistula rate was similar in the PMMF (27%) and the non-PMMF (24%) groups. Furthermore, similar durations of tube feeding, days to oral feeding, and hospitalization period were recorded in both groups.

Conclusion: The PMMF should be used judiciously as a surgical adjunct in high-risk patients, with the goal of minimizing the risk for the development of a pharyngocutaneous fistula.


As a result of the development of organ preservation strategies for patients with advanced laryngeal cancer, initial total laryngectomy (TLR) is now performed mainly in cases involving primary tumors with extensive cartilage invasion or extralaryngeal involvement of soft tissues. Patients with poor laryngeal function (incompetent larynx) at the time of diagnosis may also benefit from primary TLR, because functional recovery after nonsurgical treatment is unlikely. In case of tumor persistence or recurrence after primary radiation or chemoradiation treatment, the only remaining option for cure is surgery in the form of salvage partial laryngectomy or TLR. The type of previous treatment, extent of the tumor, and clinical condition of the patient typically determine the type of surgical procedure that is needed. Despite the reproducibility of the surgical technique of TLR, this procedure still involves a high risk for the formation of a postoperative pharyngocutaneous fistula (PCF), especially if it is performed less than 1 year after the primary radiation treatment. Traditionally, clinical studies have documented a 10% to 20% incidence of PCF after TLR. These studies are mainly based on primary TLR. During the last decade, several studies have demonstrated improvement of outcome and a higher rate of larynx preservation after chemoradiation therapy over radiotherapy alone for advanced laryngeal cancer. Because of this level I evidence, chemoradiation therapy has become the standard of care in eligible patients. However, the combination of chemotherapy and radiotherapy can result in a higher risk of PCF formation after salvage TLR. As a result, an increase in the incidence and severity of PCF has been reported in this population.

In a recent meta-analysis of 26 studies, Paydarfar and Birkmeyer identified...
surgical margins, No. (%) .50
  Negative 57 (81) 9 (81)
  Positive 12 (19) 2 (19)
  T classification, No. (%) .50
    0 2 (3) 1 (9)
    1 8 (12) 1 (9)
    2 18 (26) 2 (18)
    3 14 (21) 3 (27)
    4 27 (38) 4 (37)
  N classification, No. (%) .40
    0 62 (90) 9 (81)
    1 3 (4) 2 (19)
    2a 2 (3) 0 (0)
    2b 2 (3) 0 (0)
  Pyriform sinus involvement, No. (%) .05
    No 68 (98.5) 9 (82)
    Yes 1 (1.5) 2 (18)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); PMMF, pectoralis major muscle flap.
SI conversion factors: To convert albumin to grams per liter, multiply by 10.
Hemoglobin level, albumin level, body mass index, radiation dose, margin status, cartilage invasion, TNM stage before salvage surgery, previous tracheostomy, method of pharyngeal suturing, and pyriform sinus involvement. Patients undergoing pharyngeal closure with PMMF had a higher proportion of supraglottic tumors (45% vs 1.5%; P < .001) and a 2.56-fold higher rate of primary chemotherapy (64% vs 25%) compared with those without PMMF reinforcement, respectively (P = .03).

An analysis of variables related to the success of pharyngeal closure showed that, overall, 24% (16 of 69) of the patients in the non-PMMF group developed a PCF (P = .70). Similarly, patients undergoing primary

Patient- and surgery-related predictors of complications were studied in cases with or without PMMF. Table 1 shows the main clinical and demographic characteristics of each group. The following parameters were similar in both groups: age, sex, comorbidity index, hemoglobin level, albumin level, body mass index, radiation dose, margin status, cartilage invasion, TNM stage before salvage surgery, previous tracheostomy, method of pharyngeal suturing, and pyriform sinus involvement. Patients undergoing pharyngeal closure with PMMF had a higher proportion of supraglottic tumors (45% vs 1.5%; P < .001) and a 2.56-fold higher rate of primary chemoradiation therapy (64% vs 25%) compared with those without PMMF reinforcement, respectively (P = .03). An analysis of variables related to the success of pharyngeal closure showed that, overall, 24% (16 of 69) of the patients in the non-PMMF group developed a PCF (P = .70). Similarly, patients undergoing primary

METHODS

This retrospective case-control study was based on a review of the hospital and outpatient clinical records of 461 patients who underwent partial laryngectomy or TLR for laryngeal cancer at Memorial Sloan Kettering Cancer Center, New York, New York, between 1991 and 2006. Only patients in whom primary radiation or chemoradiation therapy failed and who required salvage TLR were included in this study. Patients undergoing partial laryngectomy, pharyngectomy, or base of tongue resection and those requiring pharyngeal reconstruction with a flap were not included in this cohort. Our study included 80 patients, 69 of whom (86%) underwent primary closure of the neopharynx after tumor resection without PMMF reinforcement (non-PMMF group). The remaining 11 patients (14%) underwent primary closure of the pharynx, which was then reinforced with PMMF (PMMF group). The clinical and demographic characteristics of the patients were recorded and analyzed retrospectively. Postoperative complications were considered “early” when they occurred within 30 days after the operation. Complications related to pharyngeal closure were measured by recording the following parameters: PCF, local wound complications, reoperation for pharyngeal reconstruction, duration of nasogastric feeding, days until full oral feeding, and duration of hospitalization. Overall, 236 variables were recorded for each patient. The comorbidity of the patients was recorded using the Charlson comorbidity index. Clinical, demographic, and tumor variables were analyzed using non-parametric qualitative and quantitative tests. The Fisher exact test (StatCalc 2.0, University of Louisiana, Lafayette) was used when the number of events was less than 10. \( \chi^2 \) Tests (likelihood ratio) and a Cox proportional hazards model (JMP; SAS Institute Inc, Cary, North Carolina) were used for comparative analysis. The study was approved by the institutional review board.

RESULTS

several significant risk factors for fistula formation. Of the 10 variables analyzed, 4 were significantly associated with PCF, including a postoperative hemoglobin level of less than 12.5 g/dL (to convert to grams per liter, multiply by 10), a prior tracheotomy, preoperative radiotherapy, and preoperative radiotherapy and concurrent neck dissection. Radiotherapy dose, time from radiotherapy to surgery, comorbid illness, tumor site, tumor stage, and concurrent neck dissection were not statistically significant. To deal with this significant postoperative morbidity, several authors have advocated routine use of a pectoralis major muscle flap (PMMF), a sternocleidomastoid muscle collar flap, or a free flap for salvage TLR, with the goal of reinforcing the primary pharyngeal suture line with vascularized tissue. The objective of our study was to report the outcomes in patients undergoing salvage TLR in whom the PMMF was used, with the goal of minimizing the risk of PCF formation.
crease in the rate of fistula in this population, the PMMF cer.10,14,20 Although radiotherapy with concurrent development of organ preservation programs of chemoradiation therapy was not reported.15 In a more re-

The rate of wound complications (hematoma, subcutaneous emphysema, and local infection) was also similar in both groups. None of the patients had a fistula that lasted longer than 30 days after the operation. Table 2 summarizes the complications and postoperative course in both groups.

Eight of the 16 patients (50%) with PCF who did not receive PMMF required a second surgical procedure for fistula closure. On the other hand, none of the patients in the PMMF group who developed a PCF required a second operation (P<.001). To identify factors associated with leaks requiring a second operation in the non-PMMF group, we further analyzed the following parameters: age, sex, operating surgeon, comorbidity index, history of alcohol and nicotine abuse, albumin level, hemoglobin level, body mass index, primary tumor site, number of subsites involved, previous chemotherapy, tumor stage, radiation dose, cartilage involvement, thyroid invasion, pyriform sinus involvement, lateral pharyngeal wall involvement, margins status, extracapsular spread, use of primary tracheoesophageal puncture, type of closure, and incidence of other complications. None of these factors were associated with major leaks requiring surgery.

Finally, to identify factors associated with PCF formation, multivariate analysis was performed on the whole study population (80 patients with or without PMMF). This analysis revealed that the only significant independent risk factor for PCF development was previous chemoradiation treatment (P = .02). Further analysis revealed that the risk for PCF formation after chemoradiation therapy was 39% compared with 21% after radiation therapy alone (relative risk, 1.83).

Because many of the patients who undergo laryngectomy require relatively long hospitalizations owing to medical comorbid conditions, we considered a duration of more than 30 days in the hospital as a prolonged hospitalization period. None of the patients with PMMF were in the hospital longer than 30 days, while 7 patients in the non-PMMF group were hospitalized longer than 30 days. If Pa and Pb are the probability for prolong hospitalization in the PMMF and non-PMMF group, respectively, then the number needed to treat (computed as 1/[pB − pA]) is 11 patients.

Table 2. Data on Complications and Postoperative Course

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-PMMF</th>
<th>PMMF</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngocutaneous fistula, No. (%)</td>
<td>16 (24)</td>
<td>3 (27)</td>
<td>.80</td>
</tr>
<tr>
<td>Fistulas requiring surgery, No. (%)</td>
<td>8 (50)</td>
<td>0 (0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>No. of fistulas persisting &gt;30 d</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Duration of nasogastric feeding, mean (SD), d</td>
<td>15 (16)</td>
<td>16 (4)</td>
<td>.80</td>
</tr>
<tr>
<td>Full oral feeding, mean (SD), d</td>
<td>10 (14)</td>
<td>12 (8)</td>
<td>.30</td>
</tr>
<tr>
<td>Hematoma, No. (%)</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>.80</td>
</tr>
<tr>
<td>Wound infection, No. (%)</td>
<td>3 (4.3)</td>
<td>1 (9)</td>
<td>.45</td>
</tr>
<tr>
<td>Subcutaneous emphysema, No. (%)</td>
<td>1 (1.4)</td>
<td>0 (0)</td>
<td>.80</td>
</tr>
<tr>
<td>Duration of hospitalization, mean (SD), d</td>
<td>16 (10)</td>
<td>17 (4)</td>
<td>.34</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; PMMF, pectoralis major muscle flap.

has been suggested as a method for buttressing the pharyngeal suture line after TLR. It was thought that the bulk of a well-vascularized nonirradiated tissue abutting the pharyngeal closure had the potential to reduce the incidence of local wound complications.

The main purpose of our study was to investigate whether the use of PMMF is associated with a lower rate of PCFs, less time to oral feeding, and reduced hospitalization time in a high-risk population. Multivariate analysis was used to identify factors associated with a higher risk of PCF formation after salvage TLR. In agreement with previous reports, we showed that prior chemoradiation therapy was associated with an 18% higher risk of fistula.4,14 However, although 64% of the patients in the PMMF group underwent prior chemoradiation therapy compared with 25% in the non-PMMF group, we found no difference in the incidence of PCF formation, local wound complications, days to oral feeding, and hospital stay between the 2 groups. As concomitant neck dissection has been shown to be associated with an increased risk of PCF formation, it is noteworthy that most of the patients in our study were node negative.

There is a large variability in the reported rates of post-laryngectomy PCF, with the incidence ranging from 2.6% to 66%.13 This variability can largely be explained by differences in study period, patient characteristics, surgeon experience, and prior therapy. Our rate of PCF formation is similar to that reported in other studies of patients undergoing salvage TLR.4,14,21-25

Several studies have specifically examined the utility of PMMF for buttressing the pharyngeal suture line after TLR. Smith et al15 compared their results with PMMF with those of a historical cohort that was surgically treated without pectoralis flaps and reported a significant reduction in the rate of PCF development (from 23% to 1%). They concluded that PMMF should become a standard technique in TLR for the prevention of PCF. In their study, only 25% of the patients had undergone previous radiation therapy, and the number of patients who received chemoradiation therapy was not reported.15 In a more re-
cent article, Righini et al\textsuperscript{16} reported their experience with patients undergoing salvage TLR (25\% of them received chemoradiation therapy) and reported a decrease in the incidence of PCF from 50\% without PMMF to 23\% with the flap. This difference, however, did not reach statistical significance. Similar results were described by Al-bimbawy\textsuperscript{17} for the sternocleidomastoid muscle flap. Recently, Fung et al\textsuperscript{18} also investigated the routine use of a free radial forearm or anterolateral thigh flaps to reinforce the pharyngeal suture line in patients undergoing salvage TLR. They reported a similar incidence of PCF in the free flap group (29\%) and their control group (30\%). These studies and the observations in our current report indicate that the risk of fistula formation in the high-risk group of patients requiring TLR is significantly reduced and is similar to that in the group of patients who were thought to have tissues that were healthy enough not to require pharyngeal suture line reinforcement with PMMF.

It is well recognized that the duration of time to closure of a PCF is longer if the tissues have been irradiated.\textsuperscript{20} In our study, 16 patients undergoing pharyngeal closure without PMMF developed a PCF, and 50\% of them required revision surgery to repair the fistula. In comparison, none of the patients in the PMMF group required a second operation. It is conceivable that the fistula in these patients was more contained and was able to be managed conservatively. Alternatively, it is also possible that patients who received a PMMF had exhausted all available reconstructive options and therefore had to be treated conservatively. However, because none of our patients developed a fistula more than 30 days after TLR, we conclude that PMMF brought healthy, nonirradiated vascularized tissue at the suture line, permitting spontaneous closure of the fistula without the need for surgical intervention. Therefore, in patients who do develop a PCF, PMMF seems to limit the severity of the fistula and reduces the need for revision surgery.

Obviously, there are several limitations related to the retrospective design of our study. First, the small number of patients who were enrolled in our study limits our ability to draw strong conclusions from the data. Second, although more than 200 items were entered in our database, the question as to what factors influenced the decision of the surgeon to perform a PMMF reconstruction is difficult to answer completely. One hypothesis is that the concern for the potential risk of fistula formation in the mind of an experienced surgeon at the time of surgery is a reasonable reflection of the increased risk for PCF. The only significant differences that we found between the 2 groups of patients were previous chemoradiation treatment and supraglottic origin of the primary tumor. Other factors such as tension on the suture line, friable pharyngeal mucosa, and fibrosis are difficult to quantify and were not available for analysis. These important variables can potentially affect the complication rate and may also influence the decision of the surgeon as to whether or not to use a PMMF.

In our study, the PMMF was used more frequently in patients with supraglottic tumors. In this group of marginal zone tumors, it is possible that closure of the residual mucosa may have needed approximation of the pharyngectomy defect under more tension than in other cases in which laryngectomy was performed for glottic tumors. It is therefore likely that subjective factors such as tension on the suture line may have contributed to an even higher risk of complications in this group.

We conclude that the PMMF should not be used as a routine procedure in patients who require salvage TLR (where the overall rate of PCF is lower than 30\%). In view of the increased morbidity, time, and cost of adding PMMF (vascularized tissue) to buttress the pharyngeal suture line, this procedure should be used judiciously in patients with prior chemoradiation treatment and in those with poor nutritional status. Also, the size of the surgical defect and the vascularity of the tissues at the pharyngeal suture line are other considerations. Therefore, in a selected population of patients at high risk for PCF, the PMMF may be a valuable adjunct for decreasing the risk of complications, morbidity, and the potential need for revision surgery.

In conclusion, previous chemoradiation treatment is an independent risk factor for PCF formation after salvage TLR. The PMMF should be used judiciously as a surgical adjunct for buttressing the pharyngeal suture line in patients who are at a high risk for PCF formation.

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Author Contributions: Drs Gil and Patel had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Gil, Kraus, Shah, and Patel. Acquisition of data: Gil, Gupta, Kummer, and Patel. Analysis and interpretation of data: Gil, Cordeiro, Kraus, and Patel. Drafting of the manuscript: Gil, Kummer, and Patel. Critical revision of the manuscript for important intellectual content: Gil, Gupta, Cordeiro, Kraus, and Patel. Statistical analysis: Gil and Patel. Obtained funding: Gil. Administrative, technical, and material support: Kummer. Study supervision: Cordeiro, Kraus, Shah, and Patel.

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REFERENCES


