Vocal Fold Paralysis after Esophagectomy for Carcinoma

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Abstract

Objectives. (1) To recognize factors that contribute to vocal fold paralysis (VFP) after esophagectomy. (2) To describe the morbidity associated with VFP after esophagectomy.

Study Design. Retrospective cohort study.

Setting. Tertiary care academic medical center.

Subjects and Methods. The medical records of 91 patients undergoing esophagectomy for malignancy were reviewed (2008-2014). Twenty-two patients with postoperative VFP were compared with 69 patients without VFP with regard to preoperative variables, surgical approach (transcervical vs other), and postoperative outcomes. A subset analysis of cervical approaches was performed, including those where an otolaryngologist assisted.

Results. There were no significant differences in preoperative variables between patients with and without VFP. Cervical approaches were associated with increased VFP ($P < .0001$). Recurrent laryngeal nerve (RLN) identification was associated with increased VFP ($P = .0001$). RLN dissection by head and neck surgeons was associated with decreased VFP ($P = .0223$). Patients with VFP had longer lengths of stay ($P = .0078$), higher rates of tracheotomy ($P = .0439$), and required more outpatient swallow evaluations ($P = .0017$). Mean time to diagnosis of VFP was 45.6 days (median, 7.5 days).

Conclusions. Cervical approaches are associated with increased VFP in patients undergoing esophagectomy for malignancy. When cervical approaches and mobilization are required, the inclusion of an experienced cervical surgeon to identify the RLN may improve the rate of postoperative VFP. Patients with VFP after esophagectomy experience significantly more morbidity. Due to the potential delay in diagnosis and treatment of postoperative VFP, routine assessment of inpatient vocal fold function may be beneficial.

Keywords

vocal fold paralysis, esophagectomy, recurrent laryngeal nerve injury, carcinoma, otolaryngologist

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Esophageal malignancy will affect an estimated 16,980 patients this year,1 the majority of whom will be initially treated with systemic chemotherapy and radiation. A small number of patients will undergo primary esophagectomy; however, most surgical candidates will undergo resection only after neoadjuvant therapy. Despite the array of treatment options, the 5-year relative survival for esophageal carcinoma remains dismal at 17.9%.1

Additionally, many of these patients suffer from decreased posttreatment quality of life, especially with regard to speech and swallowing.2 In an attempt to decrease morbidity and increase quality of life, we investigated vocal fold paralysis (VFP) in patients undergoing esophagectomy for malignancy. VFP is a well-known complication after esophagectomy, with a reported incidence of 2% to 80%.3 Factors associated with postesophagectomy VFP include annual operative volume4 and surgical approach.5-8 Postesophagectomy VFP is also associated with a variety of pulmonary complications as well as with longer stays in the intensive care unit (ICU).8,9 The goals of this study were to recognize additional factors that contribute to VFP and to further characterize the morbidity associated with VFP after esophagectomy.

Subjects and Methods

This work was approved by the institutional review board at our institution. We utilized a retrospective cohort design to compile a database from our institution’s electronic medical

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Table 1. Comparison of Preoperative Variables.

<table>
<thead>
<tr>
<th></th>
<th>VFP (n = 22)</th>
<th>No VFP (n = 69)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>67</td>
<td>64</td>
<td>.136</td>
</tr>
<tr>
<td>Male</td>
<td>19 (86)</td>
<td>62 (90)</td>
<td>.700</td>
</tr>
<tr>
<td>Mean body mass index</td>
<td>28.1</td>
<td>27.5</td>
<td>.549</td>
</tr>
<tr>
<td>Tumor location(^b)</td>
<td>20 (91)</td>
<td>67 (97)</td>
<td>.245</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>21 (96)</td>
<td>66 (96)</td>
<td>1.000</td>
</tr>
<tr>
<td>Prior chemoradiation</td>
<td>20 (91)</td>
<td>53 (77)</td>
<td>.221</td>
</tr>
<tr>
<td>Prior neck surgery</td>
<td>1 (5)</td>
<td>6 (9)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Abbreviation: VFP, vocal fold paralysis.

*Values presented as n (%) unless noted otherwise.

\(^b\)Distal esophagus.

record from 2008 to 2014. The criteria for our query utilized all available electronic medical record procedure descriptions for which esophagectomy was included. The available procedures were as follows: esophagogastrectomy with gastric pull-up (pharyngoesophagogastrectomy), esophagogastroctomy or esophagogastric resection, laparoscopy with transhiatal esophagostomy with transthoracic mobilization, laparoscopy with transhiatal esophagostomy, esophagostomy with reconstruction, and esophagostomy partial. This initial search returned records for 135 patients. Charts were reviewed to confirm the surgical procedure and malignant diagnosis and to eliminate duplicate listings. Ninety-one patients remained after exclusion.

Records were reviewed for the presence of VFP, which was defined as vocal fold immobility seen on flexible laryngoscopy after esophagectomy either during initial admission or in an outpatient clinic after discharge. In the case of delayed outpatient diagnosis after esophagectomy, etiology was attributed to surgery only after workup and exclusion of alternate diagnoses (eg, tumor recurrence). Most VFP patients were identified after otolaryngology service consultation was requested. Of note, patients who displayed symptoms suggestive of VFP but for whom laryngoscopy was not performed were not included in the VFP group. Additionally, neither manual palpation under direct laryngoscopy nor electromyography was utilized to determine VFP. The comparator group comprised those patients who underwent esophagectomy for malignant disease without diagnosis of postoperative VFP.

Charts were reviewed for demographic variables, histologic tumor type, pathologic stage, preoperative chemoradiation, previous neck surgery, surgical approach, recurrent laryngeal nerve (RLN) identification during dissection, utilization of an otolaryngologist–head and neck surgeon for cervical approaches, pneumonia, requirement for tracheotomy, inpatient and outpatient swallow evaluations (videofluoroscopic studies, flexible endoscopic evaluation of swallowing, bedside swallow evaluations, esophagrams), need for postoperative reintubation, inpatient death, total length of stay, total follow-up, and readmission within 12 months.

Categorical variables were analyzed with Fisher’s exact test and continuous variables with the Mann-Whitney U test (GraphPad Prism 6, La Jolla, California). Prior to inter-cohort analysis, preoperative patient variables were analyzed to ensure similar patient populations. P < .05 was considered statistically significant for all tests.

**Results**

Preoperative variables were similar between patients with and without VFP after esophagectomy (Table 1). Additionally, there was no significant difference in disease stage between the 2 groups (P = .4183). Between 2008 and 2014, 91 consecutive patients underwent esophagectomy for malignant disease, 22 of whom were diagnosed with VFP postoperatively (24%). Recurrent laryngeal nerve (RLN) injury was unilateral in all cases and left-sided in 21 of 22 cases (96%). Mean time to VFP diagnosis was 45.6 days (median, 7.5 days).

Postesophagectomy VFP was associated with higher rates of tracheotomy, pneumonia, reintubation, more frequent swallowing evaluations, as well as longer postoperative intubation time and overall length of stay (Table 2). Inpatient death occurred less frequently in the VFP group.

Six lead surgeons are represented in this study; the 2 busiest performed 41% and 30% of the cases. The other lead surgeons performed 12, 8, 4, and 3 cases. The majority of patients (n = 56, 62%) underwent esophagectomy utilizing cervical mobilization, 22 of whom experienced postoperative VFP (39%). When compared with other types of surgical exposure, transcervical dissection was significantly associated with postoperative VFP (P < .0001). Consequently, all patients who developed VFP had undergone a cervical approach.

During the study period, it was common to utilize 2 surgeons—one for an abdominal and/or thoracic approach and the other for cervical mobilization. Often, an otolaryngologist–head and neck surgeon was preoperatively consulted for cervical exposure. Of the 56 cases utilizing cervical mobilization, 3 otolaryngologists performed 18, 15, and 1 approaches. Operative reports were reviewed for identification of the RLN during dissection. In no case was the RLN intentionally sacrificed (ie, due to tumor involvement). For all approaches (cervical, transthoracic, transabdominal), the RLN was identified in 86% of patients with postoperative VFP, compared with 39% in patients without VFP (P = .0001). During cervical approaches, the RLN was identified in 82% of cases, and head and neck surgeons identified the RLN more frequently than other surgical specialists (97% vs 59%, P = .0005). During these cases, VFP was significantly lower when head and neck surgeons performed the dissection (30% vs 60%, P = .0223).

Thirteen patients (59%) underwent injection laryngoplasty with a temporary agent as the initial surgical management of their VFP. The average time to initial injection was 48.3 days (median, 46.0 days); however, 3 patients underwent inpatient injection laryngoplasty under general anesthesia at 6, 6, and 12 days. Twelve outpatient injections were performed in 10 patients (3 in office, 9 with direct microlaryngoscopy under general anesthesia). One patient required a type I thyroplasty after initial injection laryngoplasty. Seven patients (32%) regained vocal fold function...
Table 2. Postoperative Variables.*

<table>
<thead>
<tr>
<th></th>
<th>VFP (n = 22)</th>
<th>No VFP (n = 69)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tracheotomy</td>
<td>7 (32)</td>
<td>8 (12)</td>
<td>.0439</td>
</tr>
<tr>
<td>Reintubation</td>
<td>7 (32)</td>
<td>16 (23)</td>
<td>.4133</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 (18)</td>
<td>8 (12)</td>
<td>.4744</td>
</tr>
<tr>
<td>Outpatient swallow</td>
<td>14 (64)</td>
<td>16 (23)</td>
<td>.0017</td>
</tr>
<tr>
<td>Inpatient swallow</td>
<td>20 (91)</td>
<td>51 (74)</td>
<td>.0819</td>
</tr>
<tr>
<td>Intubation time, d</td>
<td>2.9</td>
<td>1.6</td>
<td>.2501</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>16.0</td>
<td>13.3</td>
<td>.0078</td>
</tr>
<tr>
<td>Readmission</td>
<td>9 (41)</td>
<td>23 (33)</td>
<td>.6100</td>
</tr>
<tr>
<td>Death</td>
<td>1 (5)</td>
<td>7 (10)</td>
<td>.6742</td>
</tr>
</tbody>
</table>

Abbreviation: VFP, vocal fold paralysis.

*Values presented as n (%) unless noted otherwise. Bold indicates statistical significance, P < .05.

Inpatient/outpatient swallow = at least 1 of the following studies performed: bedside swallow study, videofluoroscopic evaluation of swallowing, flexible endoscopic evaluation of swallow, esophagram.

Rate of readmission within 12 months of initial surgery.

Death during primary admission.

(partial or full) at an average of 8 months (range, 1-19; median, 6). The mean outpatient follow-up for the VFP patients was 12 months (range, 0-33; median, 12); however, this represents evaluation by a surgical oncologist, medical oncologist, or otolaryngologist. Accordingly, otolaryngology follow-up data were incomplete.

Discussion

The rate of postesophagectomy VFP in this study (24%) falls within the wide range reported in the literature (2%-80%).6-10 Multiple authors have reported on the increased rate of RLN injury associated with cervical anastomosis.5-8 Similarly, we found that cervical approaches were significantly associated with VFP.

Orringer and colleagues investigated postesophagectomy complications and the learning curve associated with operative volume. They found an inverse correlation with postoperative complications as the lead surgeon performed the index case more frequently. For example, the rate of VFP went from 32% during the first 4 years of practice (23 cases/year) to 5% after 8 years (45 cases/year), 3% after 12 years (55 cases/year), and finally to <2% (80-100 cases/year).4 Additionally, Dimick et al showed significant differences in mortality after esophagectomy between high- and low-volume hospitals and between high- and low-volume surgeons. High- and low-volume centers perform >12 and <5 esophagectomies per year, whereas high- and low-volume surgeons perform >5 and <2 esophagectomies per year, respectively.11 Accordingly, with an average of 13 esophagectomies (all types) per year during the study period, our institution would be classified as high volume. However, a subset analysis revealed an average of only 8 transcervical approaches per year performed during the same period. Although postesophagectomy VFP was significantly less when head and neck surgeons performed the cervical approach and RLN dissection, the rate of 30% in the hands of head and neck surgeons is not trivial. One possible explanation hinges on the difficulty to identify the exact site and timing of RLN injury when separate teams are used for the transcervical mobilization and subsequent resection and anastomosis, respectively. Consequently, the rate of VFP may not be entirely attributable to the transcervical approach alone but may instead be an indication of significant manipulation during resection and anastomosis. Additionally, RLN identification was significantly associated with postoperative VFP. While seemingly counterintuitive, one explanation for this finding is that RLN identification and dissection were routinely performed during cervical approaches; however, this was performed during no abdominal or thoracic approaches. Therefore, RLN identification can be viewed as a surrogate for cervical exposure in this series.

Gockel and associates reported significant morbidity associated with RLN injury after esophagectomy for carcinoma, namely postoperative pneumonia (52% vs 26%).8 In our study, postoperative pneumonia was also higher in the VFP group, however not significantly so (18% vs 12%, P = .4744). Similarly, Hulscher and colleagues found higher rates of pulmonary complications in patients with VFP after esophagectomy, leading to significantly more reintubations, prolonged ventilation time, and longer stays in the ICU.9 In line with these studies, we found a significantly higher rate of tracheotomy (32% vs 12%, P = .0439) and overall inpatient length of stay (average, 16.0 vs 13.3 days; P = .0078) for patients with postesophagectomy VFP. In contrast to our findings and those of other groups, some authors found no significant increase in pulmonary complications, ICU stay, or overall inpatient admission.10

As dysphagia and aspiration with subsequent pulmonary complications are major concerns in patients with VFP, we also investigated the necessity for swallowing evaluations (videofluoroscopic studies, flexible endoscopic evaluation of swallowing, bedside swallow evaluations, and esophagrams). Due to the prevailing practice patterns at our institution, many patients underwent a barium esophagram to evaluate anastomotic integrity prior to initiation of oral intake. We found no significant difference between VFP patients requiring at least 1 inpatient swallow study and those without postoperative VFP (91% vs 74%, respectively; P = .0819). However, we found that after discharge, patients with VFP underwent significantly more outpatient swallow evaluations than their non-VFP counterparts (P = .0017).

Attention to medical sequelae and quality of life for patients with VFP has driven an ongoing effort to elucidate optimal timing for temporary and permanent treatment. Timely diagnosis of VFP is perhaps of equal importance. The time to diagnosis in our group was prolonged (mean, 45.6 days; median, 7.5 days). Routine postoperative flexible laryngoscopy was not performed; rather, clinical symptomatology dictated evaluation and need for otolaryngology consultation. However, chart review revealed multiple patients...
whose overall clinical picture was suggestive of VFP and on whom further evaluation was not undertaken. As most of the VFP cases were diagnosed after consultation of the oto- laryngology service (vs patients with whom the head and neck service was already familiar as consultants for the surgical approach), one potential explanation for this finding was the overall practice pattern and criteria for otolaryngology consultation. There was no formal consultation protocol for postesophagectomy vocal fold evaluation. In an effort to expedite the diagnosis and treatment of postesophagectomy VFP, routine inpatient postoperative vocal fold assessment would be a simple and critical intervention. This type of evaluation would inevitably capture some cases of subclinical VFP; however, clinically significant cases would be identified quicker, and the natural history of this injury would be more accurately recorded.

The majority of VFP patients in this study underwent injection laryngoplasty, most of whom within 2 months of diagnosis. Previous studies have investigated early versus late medialization, with favorable results for patients in early cohorts. Friedman and colleagues defined early intervention as ≤6 months and found that only 37.5% of patients in the early cohort and 100% patients in the late cohort required permanent transcervical medialization procedures, respectively. One notable limitation was the small sample size of the late cohort (n = 3). Bhattacharyya et al reported decreased length of stay, number of bronchoscopies, and rate of postoperative pneumonia in patients undergoing early medialization (<4 days) for unilateral VFP after thoracic surgery. With an average time to medialization of 4.5 days after RLN injury, Graboyes and colleagues showed that early medialization can be performed safely in patients with unilateral VFP after thoracic surgery. They showed that a single injection is often sufficient to improve aspiration and dysphagia and that only 25% of patients required further treatment for persistent dysphonia. Arviso and associates evaluated the long-term outcomes of injection laryngoplasty in patients with unilateral VFP and also found that the majority of patients required only a single treatment with a temporary agent. Furthermore, they showed that the majority of patients either recovered function (partial or complete) or developed adequate glottal compensation, which obviated the need for permanent intervention. Of specific interest to our study, they found that 64% of patients with unilateral iatrogenic paralysis achieved partial recovery (12%), full recovery (12%), or adequate compensation (40%) after injection laryngoplasty. The median end point to recovery/compensation or the need for permanent medialization in their subset analysis was 11 months. In our study, the average return of function (partial or complete) was 8 months; however, follow-up data including laryngoscopy were complete in only 8 of 22 patients.

An obvious limitation of this study is its retrospective nature. Although charts were individually reviewed for accuracy (rather than reliance solely on procedural coding), rates of VFP are likely an approximation due to under- or overestimation depending on the scenario. For example, at least 1 patient experienced significant postoperative respiratory distress with stridor and required emergent reintubation. However, flexible laryngoscopy was not performed, thus making it impossible to determine if VFP was a contributing factor. Conversely, patients in this study rarely underwent preoperative evaluation of vocal fold mobility; therefore, it is conceivable that immobility could have been present preoperatively.

Conclusions

Cervical approaches are associated with increased VFP in patients undergoing esophagectomy for treatment of malignant disease. When a cervical approach and mobilization are required, the inclusion of an experienced cervical surgeon, as part of the operative team to identify the recurrent laryngeal nerve, may improve the rate of postoperative VFP. A useful scenario for this system may be in centers with lower case volume. Patients with VFP after esophagectomy experience significantly more morbidity. Due to the potential for delay in diagnosis and treatment of postoperative VFP, routine assessment of vocal fold function during the inpatient period may be beneficial.

Author Contributions

Michael J. Loochtan, design, acquisition/analysis of data, drafting/revision of work, final approval; Daniel Balcarcel, acquisition/analysis of data, revision of work, final approval; Elizabeth Carroll, acquisition/analysis of data, revision of work, final approval; Eileen M. Foecking, analysis of data, revision of work, final approval; Eric J. Thorpe, acquisition/analysis of data, revision of work, final approval; Steven J. Charous, design, acquisition/analysis of data, revision of work, final approval.

Disclosures

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References


