Esophageal Dysmotility in Patients following Total Laryngectomy

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Abstract
Objectives. Dysphagia is common in total laryngectomees, with some symptoms suggesting esophageal dysmotility. Tracheoesophageal (TE) phonation requires effective esophagopharyngeal air passage. Hence, esophageal dysmotility may affect deglutition or TE phonation. This study aimed to determine (1) the characteristics of esophageal dysmotility in laryngectomees, (2) whether clinical history is sensitive in detecting esophageal dysmotility, and (3) the relationship between esophageal dysmotility and TE prosthesis dysfunction.

Study Design. Multidisciplinary cross-sectional study.

Setting. Tertiary academic hospital.

Subjects and Methods. For 31 participants undergone total laryngectomy 1 to 12 years prior, clinical histories were taken by a gastroenterologist and a speech pathologist experienced in managing dysphagia. Esophageal high-resolution manometry was performed and analyzed using Chicago Classification v3.0.

Results. Interpretable manometric studies were obtained in 23 (1 normal manometry). Esophageal dysmotility patterns included achalasia, esophagogastric junction outflow obstruction, diffuse esophageal spasm, and other major (30%) and minor (50%) peristaltic disorders. The sensitivity of predicting any esophageal dysmotility was 28%, but it is noteworthy that patients with achalasia and diffuse esophageal spasm (DES) were predicted. Two of 4 participants with TE puncture leakage had poor esophageal clearance. Of 20 TE speakers, 12 had voice problems, no correlation between poor voice, and any dysmotility pattern.

Conclusions. Peristaltic and lower esophageal sphincter dysfunction are common in laryngectomees. Clinical history, while not predictive of minor motor abnormalities, predicted correctly cases with treatable spastic motor disorders. Dysmotility was not associated with poor phonation, although TE puncture leakage might be linked to poor esophageal clearance. Esophageal dysmotility should be considered in the laryngectomees with persisting dysphagia or leaking TE puncture.

Keywords
laryngectomy, esophagus, motility, dysphagia, achalasia, high-resolution manometry, Chicago Classification

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Total laryngectomy is performed to treat advanced or recurrent laryngeal cancer,1,2 usually followed by chemoradiotherapy.3,4 Surgery involves complete removal of the larynx as well as the hyoid bone, epiglottis, up to 2 tracheal rings, and possible destruction of the laryngeal nerve,2,5,6 resulting in permanent alterations to respiratory, phonatory, and deglutitive functions.7,8

Dysphagia following total laryngectomy is common, underreported by patients, and underrecognized by clinicians.9-11 Estimates of postlaryngectomy dysphagia range from 17% to 72%.12-14 Postlaryngectomy dysphagia is related primarily to collateral surgical damage, as well as chemoradiation-related pharyngeal neuromuscular dysfunction and pharyngoesophageal stenosis.1,3,15 Anecdotally in our clinic, laryngectomy patients, with no premorbid history of esophageal dysphagia, frequently report symptoms

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referable to the esophagus. Their symptoms may include chest pain, regurgitation, and retrosternal bolus holdup: symptoms typical of esophageal dysmotility. This observation was supported in our laboratory using standard water perfused esophageal manometry testing. However, there is a paucity of literature and lack of agreement regarding the nature and prevalence of esophageal motor dysfunction following total laryngectomy.

The gold standard for voice restoration following total laryngectomy is tracheoesophageal (TE) phonation. This is achieved by placing a 1-way silicone valve (TE prosthesis) through a tracheoesophageal puncture, which permits unidirectional airflow while preventing retrograde leakage of secretions and fluids through the tracheoesophageal puncture (TEP) into the airway. The mechanisms underpinning poor TE phonation are poorly understood, but it is speculated that esophageal “incontinence” of gas reduces pressure and flow across the pharyngoesophageal junction, thereby adversely affecting TE phonation. TE puncture leakage is also a significant problem reported in over half of TE voice users. An enlarged TE puncture has been identified to be the main reason of leakage around the TE prosthesis, but the reason for leakage through the prosthesis remains unclear. The aims of this study were to determine (a) the presence, if any, of the frequency and characteristics of esophageal dysmotility in patients following total laryngectomy; (b) whether the clinical history is sensitive in predicting esophageal dysmotility; and (c) the relationship, if any, between esophageal dysmotility and TE prosthesis dysfunction.

Methods

Patients

The study protocol was approved by the Human Research Ethics Committee of the South Eastern Sydney Local Health District of NSW Health.

Patients who had undergone total laryngectomy (with or without adjuvant chemoradiotherapy) and were assessed clinically through the Swallow Clinic or outpatient speech pathology between 2012 and 2015 were eligible to participate in this prospective observational study. The symptom of dysphagia was not an inclusion criterion. Patients were excluded if they had evidence of local cancer recurrence, any neurological disorder that could cause oropharyngeal dysfunction (eg, Parkinson’s disease, cerebrovascular accident, myopathy, amyotrophic lateral sclerosis), or history of known preexisting esophageal pathology causing dysphagia before their treatment for laryngeal cancer (eg, esophageal stricture, malignancy). Patients who had had pharyngolaryngectomy were excluded. Patients presenting with dysphagia (n = 18) were compared with 5 disease controls; patients attended the Speech Pathology clinic for potential TE voice problems but without dysphagia.

High-Resolution Manometry

Participants underwent pharyngeal high-resolution manometry (HRM) combined with concurrent fluoroscopy to assess pharyngeal deglutitive function as described previously. This was followed by esophageal HRM. Following topical nasal anesthesia, we passed transnasally a solid-state HRM catheter (Unisensor AG, Attikon, Switzerland) incorporating 25 sensors spaced at 1-cm intervals, which was positioned to span the distal esophagus and the lower esophageal sphincter (LES). Ten 5-mL water swallows were performed in the supine followed by right lateral positions. When patients were able to swallow 5 mL as a single bolus from the fluoroscopic assessment, pharyngeal bolus delivery was deemed to be adequate. Swallows not matching this criterion (ie, 5 mL barium was swallowed as multiple swallows rather than as a single bolus) were considered piecemeal (coexisting pharyngeal dysfunction) and were excluded from analysis because bolus delivery is necessary to trigger esophageal peristalsis.

Pressure signals were acquired using Medical Measurement Systems software (MMS, Enschede, the Netherlands), and the results were analyzed using the Chicago Classification v3.0 using the normative ranges previously reported for this particular catheter (Unisensor AG, Attikon, Switzerland). The proportion of patients in each category of the Chicago Classification v3.0 was summarized, noting patients with adequate bolus delivery versus those with piecemeal deglutition.

Clinical Assessment

During clinical assessment, esophageal dysfunction was considered likely to be present when patients reported at least 1 of the following symptoms: regurgitation of solids or liquids, or the sensation of a swallowed bolus “holding up” retrosternally. TE prosthesis dysfunction was defined as the presence of 1 or more of the following: (a) absent TE phonation, (b) poor-quality TE phonation (in lieu of a validated tool to grade this, we defined it as present if the patient reported it as a problem to them), and (c) leakage of secretions or fluid through or around the prosthesis into the trachea not related to valve deterioration. The relationship, if any, between TE prosthesis dysfunction and esophageal dysmotility was examined (see below) in those deemed to have adequate pharyngeal swallow delivery. (Esophageal peristalsis is only triggered if a bolus is delivered to the esophagus.) Features of esophageal dysmotility, if any, were then compared between these 2 groups.

Esophagoscopy was not performed routinely, but we do routinely perform (flexible) esophagoscopy in all laryngectomees with dysphagia.

Data Analysis and Statistics

A χ² test was used to make statistical inferences about potential differences in the frequency of different esophageal motor patterns between groups (eg, dysphagic and non-dysphagic laryngectomees, proportion of participants with and without TE prosthesis dysfunction). Fisher’s exact test was applied to determine sensitivity in detecting esophageal dysmotility by clinical assessment. All data are presented as mean and 95% confidence intervals (CIs).
Results

The 31 participants in this study had undergone total laryngectomy 1 to 12 years prior (median, 3 years) and had a mean age of 68 years, ranging from 49 to 90 years (95% CI, 65-71 years), and 74% were male. The majority (72%) had received adjuvant postoperative radiotherapy, 7% had received preoperative radiotherapy, and 14% had received adjuvant chemotherapy either preoperatively or postoperatively. Only 7% of patients had undergone surgery alone without chemoradiation. Most participants (84%) had a TE puncture and TE prosthesis. In 2 of 31 patients, manometric assessment was not possible due to severe pharyngeal strictures. In the remaining 29 patients, 6 (21%) demonstrated piecemeal deglutition (Figure 1), leaving 23 patients with interpretable esophageal HRM studies (Figure 2).

Esophageal motility was completely normal in only 1 patient. Most of the patients had minor disorders of peristalsis (50%) (Figure 3A). The second most common disorder (21.7%) was a complete loss of peristalsis in the distal 15 cm of the esophagus (Figure 3B). Two patients (8%) displayed jackhammer esophagus (Figure 3C). One patient displayed diffuse esophageal spasm (Figure 3D). One patient demonstrated the pattern of esophagogastric junction (EGJ) obstruction (Figure 3E) with relatively normal peristalsis combined with incomplete LES relaxation (integrated relaxation pressure [IRP]$_{4}$ > 29 mm Hg). One patient had achalasia type I (Figure 3F) with failed LES relaxation combined with aperistalsis (without pan-esophageal pressurization).

When comparing the disease control group with the dysphagia group, there were no significant differences between the groups in the proportion with minor disorders of peristalsis (40% vs 56%), absent contractility (20% vs 22%), or EGJ outflow obstruction pattern (1 control and 1 patient) ($P = .65$, 2-tailed, $\chi^2$). Cases of achalasia (1) and esophageal spasm (1) were confined to the group with dysphagia (n = 18) (Table 1). Inspection of Table 1 shows that even in this relatively small number of nondysphagic controls (n = 5), many of the less specific motor patterns known to be of questionable functional relevance were quite common.

Of all participants, 18 reported dysphagia. Predictably, the majority (23) reported pharyngeal dysphagia (with 6 of them unable to swallow 5 mL as a single swallow); 5 reported esophageal dysphagia, while 4 had symptoms of both pharyngeal and esophageal dysphagia. While the diagnostic sensitivity of the clinicians’ prediction of esophageal dysmotility overall was poor (28%), both significant dysmotility patterns (ie, achalasia and diffuse esophageal spasm) were predicted clinically prior to performing HRM (Table 2).

Of the 23 participants with interpretable HRM results (ie, successful intubation and adequate pharyngeal bolus delivery), 3 participants were not TE voice users. Among the remaining 20 TE voice users with interpretable HRM results, there was a wide spectrum of esophageal motility disorders, including achalasia (5%), EGJ outflow obstruction (5%), diffuse esophageal spasm (5%), jackhammer esophagus (5%), and normal motility (5%). There were 4 patients (20%) who demonstrated absent contractility and 11 patients (55%) with minor disorders of peristalsis.

Patients with TE prosthesis dysfunction (n = 12) were compared with the patients without prosthesis problems
Figure 3. Examples of high-resolution manometry tracings in 6 patients: (A) minor disorder of peristalsis, (B) absent contractility (aperistalsis), (C) Jackhammer esophagus, (D) diffuse esophageal spasm, (E) esophagogastric junction outflow obstruction, and (F) achalasia.
(n = 8) (Table 3). While achalasia (1), EGJ obstruction (1), and spasm (1) were confined to those with voice problems, there were no significant differences in proportions of patients with any peristaltic abnormality pattern between the groups (P = .94, 2-tailed, $\chi^2$), but achalasia (1), obstruction (1), and spasm (1) were confined to those with voice problems. Four of the 5 patients with leaking voice prostheses had adequate pharyngeal delivery, allowing analysis of their esophageal deglutition. Two of these 4 patients demonstrated potentially obstructive esophageal motility disorders (EGJ obstruction and spasm).

**Discussion**

In this population of patients following total laryngectomy, esophageal dysmotility was a relatively common phenomenon that was underrecognized during clinical evaluation. It is worth noting that nearly half (49%) of the patients had significant disorders of LES function or a major peristaltic abnormality, including achalasia, EGJ obstruction, diffuse esophageal spasm, jackhammer, and absent contractility. Furthermore, achalasia and diffuse esophageal spasm were only observed in patients reporting dysphagia and were accurately predicted on their clinical history. Other motility disorders were not isolated to those patients reporting dysphagia and were not readily identified during clinical consultation. There was no association between TE voice users and specific patterns of esophageal motility disorders, but poor esophageal clearance (EGJ obstruction and spasm) may be linked with leakage via the TE prosthesis.

LES abnormalities, either known to cause (achalasia) or carrying the potential for causing obstruction (EGJ outflow obstruction motor pattern), comprised 8% of the study population. It is worth noting that achalasia is a rare but readily treated motility disorder with a population prevalence of 1 in 125,000.32,33 While the present study cohort is small, our observation suggests that the incidence of achalasia may be higher than hitherto appreciated in total laryngectomy patients. Although alterations in upper esophageal sphincter function in these patients have been well documented,34-36 LES function was thought to be preserved, with the exception of 1 study that demonstrated poor LES relaxation and altered coordination during swallowing in laryngectomees.37 The findings from that study and the present study suggest that clinicians should consider this possible coexistent treatable abnormality in laryngectomees presenting with dysphagia. We acknowledge that the true prevalence of esophageal achalasia in the laryngectomy population cannot be defined in this relatively small study.

In the present study, minor peristaltic abnormalities were observed frequently (50%) and the prevalence of major peristaltic abnormalities (including absent contractility, jackhammer esophagus, and diffuse esophageal spasm) was also high (35%). However, inconsistency exists regarding the frequency and nature of esophageal peristaltic changes following total laryngectomy in published studies. Minor peristaltic changes were identified by some investigators, including decreased distal esophageal contraction amplitude and increased simultaneous nonperistaltic pressure waves.36,38-40 Other investigators reported that, despite altered proximal esophageal motility, distal esophageal peristalsis was relatively preserved.34-36 Our findings indicate that peristaltic abnormality in the distal esophagus is a true phenomenon that is commonly found following total laryngectomy.

The apparent contradiction in identification of motility disorders in total laryngectomy patients may be related in part to outdated technology used in some of these studies.34-37,39,40 such as low-resolution water perfusion techniques and multisidehole (nonsleeve) catheters that are known to underestimate failed LES relaxation.31,41 It is now well accepted that these factors lack reliability when diagnosing esophageal motility disorders compared to the systematic classification of motility disorders (Chicago Classification v3.0) using HRM.

Dysphagia following total laryngectomy is multifactorial and, in most patients, is related to pharyngeal and cricopharyngeal anatomical, postsurgical, and motor disturbances.14,42-47 The focus of clinicians on the dominance of pharyngeal symptoms means that esophageal dysfunction, if present, may not be considered in the first instance, and any symptoms arising from the esophagus may be confounded or obscured by pharyngeal symptoms. Communication difficulties in this population may also further delay diagnosis of any coexistent esophageal dysfunction. Clearly, dysphagia in the laryngectomee mandates primary investigations of pharyngeal deglutition with videofluoroscopy, esophagoscopy, and perhaps pharyngeal motility studies.3 However, the symptoms of retrosternal swallowed bolus holdup, frank esophagopharyngeal regurgitation, or TE prosthesis leakage should raise the possibility of esophageal stasis and prompt consideration of esophageal manometry.

We urge caution in interpretation of some of the less specific manometric descriptors such as “jackhammer” and minor or even major peristaltic changes. Inspection of the data in Table 1 is noteworthy in that, despite the small number of controls (n = 5), some of the motor patterns of dubious functional relevance are common in laryngectomees without dysphagia. From the management standpoint, the findings of achalasia or diffuse spasm are of major clinical relevance to dysphagia while irrespective of whether laryngectomy may or may not cause

| Table 1. Esophageal Motility Findings in Patients Referred from Clinicians with Dysphagia and Nondysphagia. |
|-----------------------------------------------|-----------------------------------------------|
| Chicago Classification v3.0 | Nondysphagia, No. (%) | Dysphagia, No. (%)a |
|-----------------------------------------------|-----------------------------------------------|
| Achalasia | 0 (0) | 1 (5.6) |
| EGJ outflow obstruction | 1 (20.0) | 0 (0) |
| Major peristaltic disorders | | |
| Diffuse esophageal spasm | 0 (0) | 1 (5.6) |
| Jackhammer | 1 (20.0) | 1 (5.6) |
| Absent contractility | 1 (20.0) | 4 (22.2) |
| Minor disorders of peristalsis | 2 (40.0) | 10 (55.6) |
| Normal | 0 (0) | 1 (5.6) |
| Total | 5 (100) | 18 (100) |

Abbreviation: EGJ, esophagogastric junction.

aThe symptom of dysphagia was based on clinical history, not fluoroscopy or other investigations.
Table 2. Sensitivity of Clinical Consultation in Detecting a Motility Disorder in Total Laryngectomy Patients Referred with Dysphagia.

<table>
<thead>
<tr>
<th>Clinical Assessed Esophageal Dysmotility</th>
<th>Esophageal HRM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported, No.</td>
<td>Achalasia</td>
</tr>
<tr>
<td>Nil reported, No.</td>
<td>Diffuse</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>Jackhammer, Absent Contractility, Minor Peristaltic Abnormality</td>
</tr>
<tr>
<td></td>
<td>All Dysphagia Patients</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>100</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>28</td>
</tr>
</tbody>
</table>

Abbreviation: HRM, high-resolution manometry.

Table 3. Esophageal Motility Results in Participants with and without TE Prosthesis Dysfunction.

<table>
<thead>
<tr>
<th>TE Prosthesis</th>
<th>No Prosthesis Dysfunction, No. (%)</th>
<th>Prosthesis Dysfunction, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achalasia</td>
<td>0 (0)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>EGJ outflow obstruction</td>
<td>0 (0)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Major peristaltic disorders</td>
<td>Diffuse esophageal spasm</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Jackhammer</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>Absent contractility</td>
<td>2 (25)</td>
</tr>
<tr>
<td>Minor disorders of peristalsis</td>
<td>6 (75)</td>
<td>5 (43)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 (0)</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>8 (100)</td>
<td>12 (100)</td>
</tr>
</tbody>
</table>

Abbreviations: EGJ, esophagogastric junction; TE, tracheoesophageal.

Esophageal dysmotility) the other descriptors have a less certain relationship to dysphagia in this population and indeed in the broader spectrum of patients undergoing esophageal manometry.48

Our clinical history was poor at predicting minor disorders of peristalsis. This is not surprising, as a long-term follow-up study of these minor peristaltic abnormalities has shown that they do not develop dysphagia.49 On the other hand, both cases of achalasia and spasm were correctly predicted by clinical history as “probable dysmotility.” Clearly in such cases, esophageal manometry is mandatory and will certainly affect management. We acknowledge limitations associated with this study. Prelaryngectomy esophageal HRM was not performed. Although we explored their preoperative history retrospectively, participants may have unreported pre-existing esophageal conditions. This fact, combined with the relatively small sample size, means that any causation between the surgery and esophageal dysmotility remains unproven. Internal bias may still exist as the study cohort was largely derived from patients with deglutition or phonation issues who are arguably more likely to participate despite the discomfort of esophageal manometry. Hence, our findings are only applicable to laryngectomees with symptoms sufficient to make them seek treatment at a clinic. Furthermore, only 4 patients had significant TE prosthesis leakage in this cohort; thus, further work to verify the putative association of leakage with esophageal clearance is required.

The pathogenetic mechanisms by which esophageal dysmotility might be related to total laryngectomy are unknown. A loss of neural inhibitory pathways underpins the motor abnormalities in esophageal achalasia. It is likely that surgical and/or radiotherapy-related damage to esophageal extrinsic or intrinsic nerves disrupts distal esophageal peristalsis and LES function.50,51 Lesions as high in the central nervous system (CNS) as the dorsal motor nucleus of the vagus can impair distal esophagus motility patterns.52 Given the location of the injurious factors in laryngectomees, damage to cervical vagal fibers is more likely to be implicated than is damage to either more proximal vagal fibers or more distal esophageal intrinsic nerves. Extrinsic vagal efferent nerve integrity is necessary for the initiation of peristalsis.53,54 Once initiated, however, ongoing propagation of peristalsis is controlled by intrinsic postganglionic esophageal nerves, which can continue propagating the process even if, under experimental conditions, one removes the influence of the distending bolus on esophageal afferents by bolus diversion, as demonstrated in an animal model.55,56 Equally important are intact afferent vagal pathways, damage to which impairs distal esophageal peristalsis and LES function. For example, pharyngeal mucosal stimulation can elicit LES relaxation.57,58 Distal esophageal peristaltic activity can also be elicited by distension of the pharynx or upper esophagus, or even electrical stimulation of the vagal afferent nerves can further support this concept. This activity even occurs when the striated muscle esophagus is prevented from contraction by blocking neuromuscular transmission with curare.59 Hence, surgical or radiotherapy-related damage to cervical vagal afferent pathways could account for our findings.

Conclusion

In conclusion, there is a significantly higher than expected proportion of patients following total laryngectomy who have esophageal dysmotility, including impaired LES function. Major dysmotility syndromes (achalasia or spasm), while rare, were observed in this relatively small prospective cohort. While the primary focus of investigation for dysphagia in laryngectomees is the pharynx, the clinician should be aware that esophageal dysphagia can coexist in these patients, and those symptoms suggestive of retrosternal holdup or esophageal liquid stasis should prompt...
esophageal manometry as the findings will influence management in a significant proportion of patients. While there appears to be no direct correlation between esophageal dysmotility patterns and impaired tracheoesophageal voice production, esophageal stasis due to dysmotility may contribute to tracheoesophageal prosthesis leakage.

**Author Contributions**

Teng Zhang, study design, manometry and videofluoroscopy acquisition, analysis and interpretation of the results, drafting and revising manuscript and final approval of the version to be published, agreement to be accountable for all aspects of the work; Julia Maclean, videofluoroscopy analysis, quality assurance, manuscript review and final approval, agreement to be accountable for all aspects of the work; Michel Szczesniak, manometry and videofluoroscopy acquisition, statistical analysis of the results, revising manuscript and final approval of the version to be published, agreement to be accountable for all aspects of the work; Paul P. Bertrand, interpretation of the results, manuscript review and final approval, agreement to be accountable for all aspects of the work; Harry Quon, interpretation of the results, manuscript review and final approval, agreement to be accountable for all aspects of the work; Raymond K. Tsang, interpretation of the results, manuscript review and final approval, agreement to be accountable for all aspects of the work; Peter I. Wu, interpretation of the results, manuscript review and final approval, agreement to be accountable for all aspects of the work; Peter Graham, interpretation of the results, manuscript review and final approval, agreement to be accountable for all aspects of the work; Ian J. Cook, study design and project supervision, data acquisition by performing endoscopic dilatations, revising manuscript and final approval, agreement to be accountable for all aspects of the work.

**Disclosures**

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