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# State of the art: Rehabilitation of speech and swallowing after total laryngectomy

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ABSTRACT

Despite the development and expansion of non-surgical organ preservation therapy, total laryngectomy continues to be the optimal therapy for far-advanced local disease and the only curative option for radiotherapy failures not amenable to partial laryngeal procedures. Laryngectomy, however, remains a life-altering operation with profound effects on swallowing and speech. In the nearly 150 years since the first total laryngectomy was performed, few ablative aspects have changed, but reconstructive techniques have undergone radical evolution. This review will trace the origins of laryngeal rehabilitation for voice and swallowing, the current state of the art with attention to pre-treatment considerations and post-operative management, current surgical management techniques, and the future of functional laryngeal reconstruction.

## Introduction

In 2018, a projected 13,150 new cases of laryngeal cancer will be diagnosed in the United States and a further 3710 will die of this disease [1]. Although definitive non-surgical therapy has become the preferred treatment for many of these patients, total laryngectomy continues to have an important role in both the primary and salvage treatment of advanced laryngeal and hypopharyngeal cancer [2,3]. In the primary setting, patients with T4a disease undergoing laryngectomy with adjuvant therapy demonstrate significantly improved local control and survival as compared with definitive non-surgical therapies and these findings are reflected in national guidelines [4]. In the salvage setting, over 60% of patients undergoing salvage laryngectomy after prior radiotherapy achieve long-term disease control and most can develop intelligible tracheoesophageal speech and maintain an oral diet [5]. Furthermore, in patients rendered disease-free but functionally debilitated by the late effects of definitive chemoradiotherapy, laryngectomy offers an option to restore both speech and swallowing.

With the continued role of total laryngectomy in the current management of laryngeal cancer, optimizing post-laryngectomy function becomes paramount. Since the earliest laryngectomies performed in the 1870s, although *peri*-operative outcomes have improved with advances in antibiotics and antisepsis, the ablative aspects of the procedure have not substantially changed [6]. The reconstruction and rehabilitation of laryngectomy defects, however, have evolved considerably. With the advent of free tissue transfer, extensive pharyngeal defects including long circumferential segments can be reliably repaired in a single stage operation. Alaryngeal voice options have expanded, as well, including esophageal speech, use of the electrolarynx, and the tracheoesophageal prosthesis. Nonetheless, laryngectomy patients remain obligate neck breathers and although many achieve excellent alaryngeal voice, tracheoesophageal prostheses require continued maintenance and are subject to valve failure and leakage. These challenges are magnified by the tumor burden or prior treatment effects of current laryngectomy patients. Presently in the United States, most patients undergoing laryngectomy have either extensive primary disease or have undergone chemoradiotherapy with disease recurrence or have such severe treatment effects that they are functionally debilitated. This review will discuss the current state of the art in post-laryngectomy swallowing and voice restoration in this challenging population and examine the future directions and developments in laryngeal rehabilitation.

## Swallowing

In normal physiology, swallowing is accomplished by alterations in pressure dynamics. Briefly, tongue base and pharyngeal contraction exert positive pressure on the bolus while simultaneous hyolaryngeal excursion anteriorly and superiorly open the pharyngoesophageal

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segment allowing the bolus to enter the cervical esophagus. In laryngectomy patients, tongue base interaction with pharyngeal wall contraction must overcome the resting pressure of the closed pharyngoesophageal segment for boluses to enter the esophagus. This change in physiology is a set up for dysphagia causing slow bolus transit or accumulation of neopharyngeal residue and is more prevalent in patients who have already received chemoradiation therapy.

*Peri-operative considerations to limit post-laryngectomy dysphagia*

While the majority of patients who undergo total laryngectomy can maintain an oral diet, the incidence and adverse effects of long-term post-laryngectomy dysphagia can be substantial. Over 40% of post-laryngectomy patients may experience subjective dysphagia in long-term follow up [7]. Further, these patients suffer significant perceived disability and distress as compared with laryngectomy patients who are able maintain an unrestricted diet. Several factors account for these differences and in particular, radio- or chemoradiotherapy has a significant detrimental effect on post-laryngectomy swallowing [8]. Dysphagia, however, is multifactorial and swallowing outcomes depend on both treatment- and patient-related factors, including surgical technique, pre-operative and adjuvant therapies, and comorbid conditions.

For this reason, to limit the incidence or severity of symptoms, it is essential to understand the modifiable factors related to post-laryngectomy dysphagia. In particular, considerable effort has been made to correlate reconstructive methods in laryngectomy closure with swallowing outcomes. Reconstructive techniques, however, including the type and levels of pharyngeal closure, vary widely across institutions [9]. Nonetheless, certain technical aspects of pharyngeal reconstruction have been associated with long-term swallowing function.

Consistently, patients requiring circumferential pharyngeal resection have an increased incidence of post-laryngectomy neopharyngeal stenosis and slow pharyngeal bolus transit, particularly in the distal anastomotic region, and resulting dysphagia as compared with those undergoing only partial pharyngectomy [7,10–12]. These patients often complain of obstruction of solid foods and medications and slow transit of liquids causing reduced oral intake and increased duration of mealtimes (Fig. 1). Free jejunal reconstruction in such cases, compared with tubed fasciocutaneous flaps, may decrease the incidence of post-operative stricture [13]. This is partially related to the decreased incidence of fistula in jejunal patients as stricture is a frequent subsequent complication of fistula. Enteric flaps, however, come with added donor site morbidity. Although intra-abdominal complications are uncommon, they can be significant, including wound dehiscence, intraperitoneal bleeding, bowel obstruction, and hernia [14]. Deglutition in enteric flaps, such as the jejunal free flap, can also be adversely affected by ill-timed peristalsis which can be problematic even when the flap is inset along the direction of natural peristalsis. Similarly, the secretory nature of the mucosa, initially thought to be beneficial, can be limiting by resulting in problematic pooled secretions. Patients with gastric pull-up reconstructions can be prone to frequent and voluminous regurgitation secondary to pooling of material in the patulous transferred stomach.

For patients who do not require circumferential pharyngeal resection, however, the amount of residual pharyngeal mucosa sufficient for primary closure has been a subject of controversy. Early authors advocated empiric cutoffs based on personal experience, such as closure over a 40Fr bougie or 3 cm of stretched native mucosa [15,16]. Few studies have addressed this question systematically, however. Hui, et al. [17] reported on 52 patients undergoing laryngectomy with primary closure, measuring the width of the remnant pharyngeal mucosa in both the relaxed and stretched positions. These authors found no correlation between post-laryngectomy dysphagia and pharyngeal mucosal width. In two patients, as little as 1.5 cm of mucosa in the relaxed position, or 2.5 cm stretched, was sufficient in for primary closure. Despite a luminal diameter of 0.8 cm, and a cross-sectional area of only 0.5 $cm^2$,

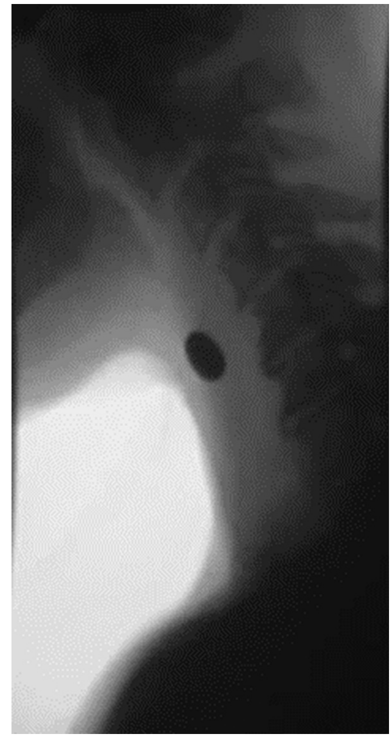

**Fig. 1.** Post-laryngectomy videofluoroscopy demonstrating a pill stuck in the neopharynx after prior pharyngeal reconstruction.

these patients had excellent post-operative weight gain and no post-laryngectomy dysphagia. In a follow up study, Hui et al. [18] performed objective swallowing measures on patients 8–10 years after laryngectomy to correlate neopharyngeal size with long-term dysphagia. For patients with a remnant pharyngeal mucosal width of 1.8–5.0 cm in the relaxed position, or 3.0–8.0 cm in the stretched position, prior to primary closure during laryngectomy, no significant relationship could be identified between the neopharyngeal size and long-term swallowing function.

While there is certainly a theoretical limit of pharyngeal width below which significant stenosis and dysphagia will occur, larger neopharyngeal size does not necessarily correlate with improved swallowing outcomes. This is likely a result of reduced bolus propulsion in the post-laryngectomy neopharyngeal conduit. An efficient swallow is not solely a function of pharyngeal diameter, but a concerted process of tongue base and progressive pharyngeal wall contraction, raising pharyngeal pressure and creating a propulsive force on the food bolus. Furthermore, a post-surgical pseudoepiglottis which traps residue can decrease swallow efficiency, particularly of solid consistencies [12]. Maclean, et al. [19] performed combined videoradiography and manometry on 24 laryngectomy patients, and found improved intrapharyngeal pressures and reduced post-swallow residue in those who had undergone closure of both the mucosa and the pharyngeal constrictors as compared with mucosal closure alone. While reapproximation of the pharyngeal constrictors can also lead to pharyngoesophageal spasm (PES) and limit tracheoesophageal speech, this study highlights the importance of physiological reconstruction when possible. When sufficient residual pharyngeal mucosa is available for primary closure, such physiological reconstruction should incorporate functional constrictor musculature to improve pharyngeal tonicity. To balance improving pharyngeal function with limiting PES, reconstructive options include the half-muscle closure or a full constrictor reapproximation with a unilateral pharyngeal plexus neurectomy [20,21]. Stronger lingual propulsion of boluses can sometimes overcome increased resistance within the neopharynx provided the tongue base is not involved in the resection or hypoglossal function has not been disrupted by late radiation effects.

### *Post-operative considerations in the management of post-laryngectomy dysphagia*

#### *Recurrence*

Despite appropriate primary laryngectomy and adjuvant therapy, over 10% of patients with T4a laryngeal cancer will have locoregional recurrence [22]. Similarly, in those undergoing salvage laryngectomy after primary chemoradiotherapy, as many as 25% will experience locoregional failure [23]. For patients with post-laryngectomy dysphagia, the underlying etiology in a significant proportion of cases may be disease recurrence [17,24]. However, in an effort to study management of treatable causes of dysphagia in survivors, reports evaluating post-laryngectomy dysphagia often exclude patients with locoregional recurrence from analysis [25]. For these reasons, the most important first step for the patient with new-onset post-laryngectomy dysphagia is to rule out recurrent disease. Physical exam, imaging (including pharyngogram), and rigid endoscopy are critical in this assessment.

#### *Neopharyngeal diverticulum*

First described in the 1960s, the anterior neopharyngeal diverticulum occurs as an outpouching of mucosa under the tongue base, resembling a pseudovallecula and pseudoepiglottis, which can lead to post-laryngectomy dysphagia and regurgitation of undigested foods (Fig. 2) [26]. While the etiology is uncertain, and such diverticulae may be related to post-operative fistula, they are more likely a by-product of pharyngeal closure technique, being more commonly seen after vertical closure compared with T-shaped closure [27]. These diverticulae are rarely symptomatic, but can reliably be treated with surgical excision when necessary. Although open approaches have been described, these diverticulae can be easily managed with a transoral approach to resect the posterior wall of the diverticulum sac, marsupializing it into the neopharyx [26,28,29].

#### *Stricture/stenosis*

Symptomatic neopharyngeal or esophageal stricture may occur in up to 20% of post-laryngectomy patients and are more common in those requiring tubed pharyngeal reconstruction (Fig. 3) [30]. These can be effectively treated with dilation and while some will require only a single dilation, most patients will require several procedures to maintain adequate swallowing [31]. For refractory strictures, adjuvant therapy with topical agents such has mitomycin C has been described [32]. For patients requiring frequent procedures, home dilation can be safely learned and is well-tolerated [33]. As a last option, surgical correction of the pharyngoesophageal stricture can be attempted. While this can be highly successful, such procedures require regional or free tissue reconstruction and come with the associated risk and morbidity of complex re-operation in a previously treated field [34]. Importantly, as post-laryngectomy dysphagia is often multifactorial including globalized dysfunction and treatment-related fibrosis, patients must obtain at least temporary symptomatic improvement from endoscopic dilation to be considered candidates for surgical repair.

**Fig. 2.** Post-laryngectomy barium swallow demonstrating anterior neopharyngeal diverticulum (arrow head) and resulting pseudo-epiglottis (arrow).

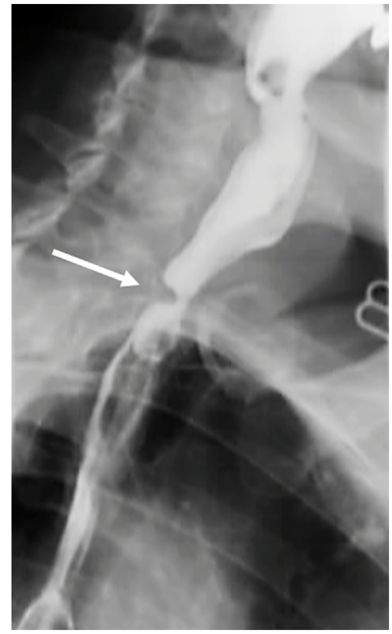

**Fig. 3.** Post-laryngectomy barium swallow after tubed pharyngeal reconstruction demonstrating distal anastomotic stricture (arrow) at the junction of the neopharynx and cervical esophagus.

Stricture and stenosis may also be related to post-operative pharyngocutaneous fistula. Post-operative pharyngeal dehiscence results in granulation tissue and healing by secondary intention which may lead to scar contracture in that region and an increase the risk of stricture [35]. For this reason, minimizing post-laryngectomy pharyngocutaneous fistula may improve long-term swallowing outcomes. This is particularly relevant with modern definitive chemoradiation protocols, which have improved survival and organ preservation in those rendered disease-free, but have substantially increased tissue toxicity and risk of wound breakdown in patients requiring salvage laryngectomy [36]. Vascularized reconstruction in such post-chemoradiation cases, whether patch or interposition grafting, may limit the incidence, duration, and severity of pharyngocutaneous fistula after salvage laryngectomy [37–39].

#### *Reduced neopharyngeal swallow efficiency*

Surgical disruption of the pharyngeal constrictors and radiation-related fibrosis results in a discoordinated post-laryngectomy swallow in which the base of tongue must assume a greater role in bolus propulsion. While incorporation of functional constrictor musculature in pharyngeal reconstruction may improve pharyngeal tone and swallow efficiency, management of post-laryngectomy reduced neopharyngeal bolus propulsion is primarily behavioral modification. This may include dietary adjustment and strengthening of the tongue base to compensate for impaired pharyngeal contraction. Early intervention by speech-language pathologists may help to improve swallowing function and limit long-term dysphagia and weight loss [40].

## Speech

### *Options for alaryngeal speech*

#### *Esophageal speech*

Esophageal speech in the laryngectomy patient is achieved by trapping air in the cervical esophagus and then voluntarily expelling the air, leading to sound production through vibrations in the neopharyngeal mucosa which can be shaped into speech by the tongue and lips. Air can either be injected or inhaled into the cervical esophagus. Injection requires a coordinated effort of the tongue and pharyngeal musculature to force air retrograde into the neopharynx and past the upper esophageal sphincter (UES). Alternatively, esophageal speakers may learn to inhale esophageal air by voluntarily relaxing the UES. Negative intrathoracic pressure created during normal inspiration can allow air to be drawn from the oral cavity past the relaxed UES and into the cervical esophagus.

Esophageal speech has the distinct advantage of allowing both hands-free and device-free verbal communication. Although speech is limited by a relatively short phonation time, low intensity, and few syllables expressed per breath, for excellent speakers it is both efficient and highly cost-effective [41,42]. The most important disadvantage, however, is the significant amount of training and motivation necessary to acquire conversational esophageal speech. Even prior to the availability of the tracheoesophageal prosthesis, at most two-thirds of laryngectomees ever attained fluent esophageal speech [43]. While esophageal speech is currently infrequently used, it remains an important method of alaryngeal communication, particularly in settings where the cost or maintenance of tracheoesophageal prostheses or the electrolarynx are prohibitive.

#### *Pneumatic or electrolarynx*

The first recorded description of an artificial larynx was pneumatic in design and originally created for voice in the setting of laryngeal stenosis prior, even, to the earliest laryngectomy. In 1859 a Czech physiologist, Johann Cerzmak, developed a reed-based device to shunt air from a tracheostomy tube into the mouth, allowing for pneumatically-driven alaryngeal speech [44]. While similar modern pneumatic artificial laryngeal devices are still available, they have the disadvantage of being conspicuous, requiring significant manual dexterity for use, and may become obstructed by tracheal secretions or saliva.

The electrolarynx has a distinctly different mechanism of action from pneumatic devices. Electrolaryngeal speech does not depend on airflow, but instead mechanically vibrates the pharyngeal tissues which leads to sound production. The earliest commercially available electrolarynx was produced in the 1920s but was large and required the user to be stationary. It was not until 1959 that the first portable electrolarynx was developed. This device was placed on the neck, causing vibrations which were transmitted to the pharynx for sound production and then shaped into speech by the tongue and lips [45]. An intraoral version of the electrolarynx was subsequently developed in the 1980s in which a tube extending from the device was inserted into the mouth to vibrate the oral cavity or pharyngeal mucosa.

The direct mechanical vibration of intraoral devices leads to a higher sound intensity and can improve speech quality. The intraoral electrolarynx is also particularly useful for patients with severe treatment-related change to the neck which precludes use of the external device. The main disadvantage of the intraoral option is the required intraoral tube which can become obstructed by secretions and can interfere with articulation. A denture-mounted device is now commercially available which may overcome these limitations. The UltraVoice (UltraVoice, Inc, Newtown Sq, PA) electrolarynx is built into an upper denture or orthodontic retainer and is controlled through a wireless hand-held switch. Ultimately, however, both external and intraoral electrolaryngeal speech is limited by its acoustic quality. Device vibrations lead to a monotone mechanical speech and although pitch control is possible with modern devices, fluent changes in intonation remain a challenge and an active area of current investigation [45].

#### *Tracheoesophageal speech*

Tracheoesophageal speech was also recognized as a potential modality for alaryngeal communication prior to the advent of total laryngectomy. In the 1840s, traumatic tracheoesophageal fistulae in tracheostomy-dependent patients were found to enable voice production [46]. Subsequently, with the first description of total laryngectomy in 1873, tracheoesophageal speech was an immediate consideration and specialized tracheostomy tubes were developed with pharyngeal cannulas for alaryngeal voicing [47]. Over the following 100 years a multitude of different techniques to achieve pulmonary flow-driven speech were theorized and tested. These included prosthetic laryngeal substitutes, the near-total laryngectomy with a functional tracheoesophageal shunt, and various neoglottic procedures with passive tracheopharyngeal connections [48–51].

All of these attempts were limited, to various extents, by resulting complications including significant aspiration, prosthesis rejection, wound breakdown, and shunt closure. In an effort to overcome these challenges, in 1980 Singer and Blom described an endoscopic technique for insertion of a valved tracheoesophageal prosthesis (TEP), allowing air passage from the tracheostoma into the pharynx but preventing aspiration of food and liquid [52]. While TEP placement carries its own potential complications including device failure and leakage, it is highly reliable and reproduceable. It has been widely adapted and modified since its inception and has been compared in numerous reports to both esophageal and electrolaryngeal speech. In a recent review of 26 articles evaluating all three modalities of alaryngeal voice, tracheoesophageal speech had significantly improved acoustic and perceptual outcomes [53]. Significant benefits were found in maximal phonation time and intensity as well as vocal quality, intelligibility, and voice-related quality of life.

### *Tracheoesophageal speech*

#### *Pre-operative considerations*

To acquire successful TEP speech, TEP placement must be safe and feasible, the patient must have the motivation and physical capacity for prosthesis use, including the appropriate manual and visual dexterity, and finally, the patient must have the resources and reliability for continued prosthesis maintenance and modification when necessary. Tracheoesophageal prosthesis placement in both the primary and secondary settings have been shown to be safe, and while complications are common after TEP placement, the majority are minor and can be managed conservatively [54,55]. The tracheostomal tissue quality should be assessed carefully, however, as those patients with particularly severe radiation effects may be at higher risk for rare serious complications such as peristomal tissue necrosis, abscess, or cervical osteomyelitis [56]. Tracheoesophageal prosthesis placement is almost always feasible and is rarely limited by patient anatomy. In patients with kyphosis or radiation fibrosis limiting neck extension, TEP placement can be performed in the office through transnasal esophagoscopy or in the operating room through use of flexible esophageal stents [57,58]. One important consideration is stomal size, however, and tracheostomal stenosis to a diameter less than approximately 1.5 cm can limit prosthesis insertion and create challenges with cleaning and prosthesis modification [59].

In patients who undergo TEP placement, approximately 80% achieve tracheoesophageal speech. Predictive factors for successful TEP use are variably reported, and tracheoesophageal speech failure is often multifactorial [60]. The physical requirements for TEP use are minimal, including vision and manual dexterity to occlude the stoma, and these functions can be accomplished by a willing caretaker as well. Patients also must have sufficient pulmonary reserve for successful TEP voicing, which requires higher driving pressures than standard laryngeal speech.

Finally, patients must be psychologically ready for the effort and care required for TEP use and maintenance, including any necessary subsequent interventions to optimize TEP voicing [61]. Initial TEP failure is often related to PES or proximal neopharyngeal stricture, both of which can be successfully addressed with secondary procedures [62].

*Primary vs secondary TEP placement*

Tracheoesophageal puncture was initially described as a secondary procedure performed at least 4 weeks after laryngectomy in which a catheter stented the surgically created tracheoesophageal fistula and a voice prothesis was placed several days later [52]. Primary tracheoesophageal puncture was adopted shortly after and in subsequent years voice prosthesis placement was performed directly at the time of laryngectomy, avoiding the need for catheter stenting with its associated inconvenience and risk of fistula tract or esophageal erosion [63,64]. Primary TEP placement avoids the need for multiple procedures and enables early voice acquisition which may improve long-term tracheoesophageal speech outcomes [65,66].

In a recent national cohort study, however, only 7% of patients undergoing total laryngectomy received a primary TEP [67]. While the reasons for this are likely multifactorial, there are few absolute contraindications to primary TEP placement. Disruption of the tracheoesophageal party wall, either inadvertently, or as part of an esophagectomy and esophageal reconstruction precludes primary TEP placement given the increased risk of mediastinitis. Apart from contraindications, however, multiple other considerations are involved in the timing of TEP placement including surgeon experience, institutional support, and perioperative complication risk. In particular, there is some concern in the literature that primary TEP placement may increase the risk of pharyngocutaneous fistula, as demonstrated in a recent meta-analysis of 11 case series comparing outcomes of primary and secondary TEP placement [68]. While it has been postulated that primary TEP may disrupt the vascular supply to the pharyngeal mucosa leading to wound breakdown, not all centers have found an such association with TEP placement and post-operative fistula [54,69,70].

In most reports, primary and secondary TEP placement have been shown to be safe and feasible in both upfront and salvage laryngectomy, those undergoing complex pharyngeal reconstruction, and when post-operative radiotherapy is required [54,71–73]. The timing of TEP placement must, therefore, balance the advantages of primary placement, the possible increased risk of pharyngocutaneous fistula, institution-specific experience, and the patient's needs and resources (Table 1). Secondary TEP placement can also be reliably performed in the office setting under local anesthesia at many institutions [57]. A final important consideration is that although adjuvant radiotherapy after primary TEP placement does not appear to increase TEP-related complications or affect long-term tracheoesophageal speech outcomes, the acute toxicities of radiation generally limit TEP usage and functional communication scores during treatment [54,74]. For this reason, in our practice, patients undergoing primary laryngectomy are usually selected for secondary placement and those patients who do receive radiotherapy after TEP placement must have realistic and appropriate expectations.

*Pharyngoesophageal spasm*

Despite the overall success of TEP placement in achieving alaryngeal voice, muscular spasm of the reconstructed pharyngoesophageal segment can significantly limit tracheoesophageal speech (Fig. 4). Such voice-limiting PES has been reported in over 30% of patients undergoing laryngectomy with reapproximation of the pharyngeal constrictors and is significantly lower in those undergoing operative interventions to prevent spasm [75]. These interventions, at the time of laryngectomy, include pharyngeal constrictor myotomy, pharyngeal plexus neurectomy, non-muscle closure, and half-muscle closure.

Pharyngoesophageal spasm as an etiology of tracheoesophageal speech failure was recognized shortly after the introduction of TEP placement. Both pharyngeal plexus blockade with lidocaine injection and videofluoroscopy demonstrated in a significant proportion of these patients that PES was directly linked to TEP speech limitation [76]. The first described intervention was secondary constrictor myotomy, requiring transection of the pharyngeal constrictors from the tongue base to the esophageal inlet [77]. Although this technique is highly successful in restoring tracheoesophageal voice in appropriately selected patients, the procedural risks are substantial including unplanned intraoperative pharyngotomy and subsequent pharyngocutaneous fistula [78]. Primary pharyngeal constrictor myotomy at the time of laryngectomy was subsequently adapted for PES prevention but comes with similar concerns regarding risk of post-operative pharyngocutaneous fistula [79].

To overcome these challenges, several techniques were developed which aim to prevent PES at the time of laryngectomy without increasing the risk of fistula. Pharyngeal plexus neurectomy is performed unilaterally and achieves permanent paralysis of the ipsilateral constrictor and cervical esophageal musculature (Fig. 5). This allows primary re-approximation of the constrictors to provide a vascularized tissue layer over the pharyngeal closure, while limiting post-operative PES without creating symptomatic dysphagia or gastroesophageal reflux [80]. Persistent PES may still be found in 10–20% of patients, however bilateral plexus neurectomy creates an atonic neopharyngeal conduit and may increase the risk of post-operative dysphagia [81]. Unilateral neurectomy has the additional advantage of creating a higher fundamental frequency of tracheoesophageal speech and a greater pitch range than pharyngeal constrictor myotomy, likely related to remaining pharyngoesophageal tone [80,82]. Pharyngeal plexus neurectomy may also be performed secondarily but post-surgical scar substantially increases the technical difficulty of the procedure and the pharyngeal neural plexus may not be identifiable [80].

Half-muscle closure was subsequently described, in which the unilateral constrictor musculature is tacked over the pharyngeal closure while the contralateral constrictors are over-sewn. Similar to pharyngeal plexus neurectomy, the half-muscle closure achieves both vascularized coverage of the pharynx and disruption of the pharyngeal

**Table 1**
Benefits and drawbacks of primary and secondary TEP placement.

| | Primary TEP | Secondary TEP |
|---|---|---|
| Benefits | 1. Avoids multiple procedures<br>2. Early voice acquisition<br>3. Ease of placement at time of laryngectomy | 1. Possible decreased rate of salivary fistula<br>2. Allows time for patients to consider the increased maintenance and financial needs of TEP usage<br>3. Optimal position placement after healing is complete<br>4. Allows recovery after adjuvant XRT or CRT<br>5. Can be performed in the office setting under local anesthesia |
| Drawbacks | 1. Possible increased rate of salivary fistula<br>2. Limited usage during acute effects of adjuvant radiation<br>3. Migration of suboptimal prosthesis position with post-operative healing.<br>4. Challenging maintenance if receiving Adjuvant XRT or CRT | 1. Delayed speech acquisition<br>2. Patients may not get TEP placed secondarily due to lack of motivation or desire to avoid further procedures<br>3. Possibility of difficult placement due to treatment-related changes |

**Fig. 4.** Post-laryngectomy spasm of the proximal pharyngoesophagus during attempted tracheoesophageal vocalization demonstrated through videofluoroscopy (left, white arrow) and clinical examination (right, black arrow).

muscular ring, limiting post-operative PES [20]. Finally, non-muscle closure has been reported which consists of pharyngeal mucosal and submucosal closure alone without re-approximation of the pharyngeal constrictors. While this has been shown to decrease pharyngoesophageal segment pressures without increasing the risk of pharyngocutaneous fistula, theoretical concern remains regarding the risk of pharyngeal breakdown for a single-layer pharyngeal closure [83,84].

Despite operative prevention of PES, TEP speech failure may still occur in over 10% of patients, commonly due to voice-limiting spasm or neopharyngeal stricture [62]. Videofluoroscopy is an excellent initial diagnostic test and in-office injection of the pharyngeal constrictors with local anesthetic will often confirm PES as the underlying etiology. In an effort to achieve pharyngoesophageal relaxation without operative intervention and associated risks of secondary myotomy or neurectomy, several authors in the early 1990s reported injecting Botulinum toxin A (Botox) into the unilateral constrictor musculature, providing long-term pharyngoesophageal relaxation [85–87]. A typical regimen consists of 50-100U divided into several aliquots injected under EMG guidance along the pharyngeal constrictors. This procedure achieves TEP speech improvement in greater than 80% of patients, and those who fail initial therapy often benefit from repeat injection [88]. In addition, while the biological effects of Botox dissipate after several months, many patients do not require further treatment, a phenomenon thought related to a learned ability to voluntarily relax the pharyngoesophageal segment, facilitated by initial Botox chemodenervation [89]. Given the ease and safety of administration, Botox has replaced operative intervention as the primary management option for post-laryngectomy PES.

*TEP speech following laryngopharyngectomy and pharyngeal reconstruction*

Tracheoesophageal prosthesis placement has been demonstrated to be safe and effective even the setting of complex pharyngeal reconstruction. While tracheoesophageal speech in these patients is generally intelligible, perceptual and acoustic speech outcomes are often inferior in comparison to patients undergoing primary pharyngeal closure after laryngectomy alone [90–92]. Reconstructive choices, however, do not appear to significantly affect voice. Despite differences

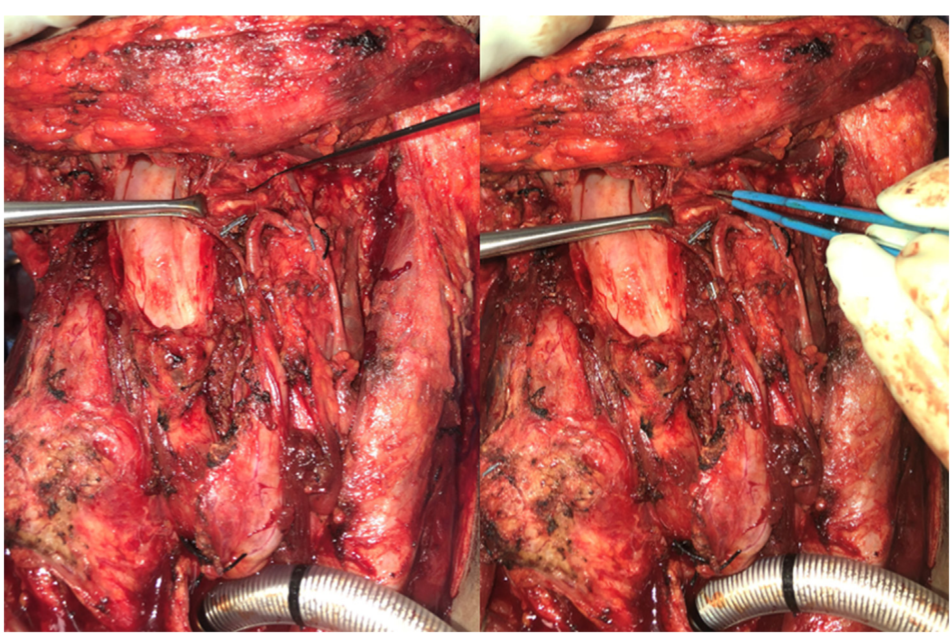

**Fig. 5.** The pharyngeal neural plexus is identified between the constrictor musculature and carotid sheath and confirmed with nerve stimulation (left). The neural plexus can then be divided proximally with a jeweler's tip bipolar (right).

in tissue pliability and composition, patients undergoing radial forearm, anterolateral thigh, and jejunum free flaps for circumferential pharyngectomy defects demonstrate similar quantitative and qualitative tracheoesophageal speech outcomes [92,93].

In addition to affecting tracheoesophageal voice, extensive pharyngeal resection has also been reported as an independent risk factor for TEP-related complications [94]. While this increased risk should not preclude TEP placement in such patients, it remains an important consideration in patient counseling and decision-making. This concern has led some authors to move to secondary TEP placement after adequate pharyngeal healing in patients undergoing total laryngopharyngectomy [94,95]. The benefits of this approach remain controversial, however, as other centers have found no such increased risk of complications and excellent speech outcomes in patients undergoing primary TEP placement concurrently with complex pharyngeal reconstruction [72,73,96].

Patients requiring cervical esophagectomy and esophageal reconstruction, however, require second TEP placement due to disruption of the tracheoesophageal party wall and associated risks of mediastinitis for primary TEP placement. Despite the increased anatomical complexity, TEP in such patients has been shown to be safe and effective done secondarily either under general anesthesia or in the office through a transnasal esophagoscopy approach [97,98].

*Troubleshooting problems with TEP speech*

Despite advances in TEP design including the development of indwelling prostheses, magnetized valves, and antimicrobial materials, device complications are common. Leakage through the prosthesis is the most frequent indication for replacement, and in a recent review of TEP durability, the median lifetime of an indwelling prothesis was only 70 days [99]. This is in stark contrast to historical data suggesting *in situ* prosthesis duration of greater than 6 months in the majority of patients [100]. Although the underlying cause of the shorter prothesis lifetime in recent years remains unclear, these data are essential to patient counseling and treatment planning. It is worth noting that prosthesis management in the era before the introduction of the indwelling-type prosthesis – which are standardly placed by health care professionals – was patient-based and prostheses were routinely removed, cleaned and replaced by the patient at home. Such routine care helped prevent biofilm and fungal deposition, factors significantly linked to prosthesis failure (Fig. 6). Extending device lifetime will be a critical area of future research as specific devices with unique modifications, such as the Provox ActiValve (Atos Medical Inc, New Berlin, WI), may have significantly greater durability, but at much higher cost [99].

In addition to valve failure and subsequent leakage through the device, leakage may also occur around the prosthesis due to fistula tract enlargement [55]. While this complication can be severe, resulting in aspiration pneumonia or feeding tube dependence, the majority of patients can be managed with conservative measures. Successful conservative management of tracheoesophageal fistula tract enlargement often requires a combination of several techniques which may include use of a prosthesis with enlarged tracheal and/or esophageal flanges, temporary prosthesis removal with subsequent tract contracture, submucosal purse-string sutures, or injectable augmentation with resorbable or non-resorbable fillers (Fig. 7) [55,101,102]. Careful attention should also be given to potentially reversible medical issues such as hypothyroidism, malnutrition, and poorly controlled diabetes. Additionally, in patients with intractable *peri*-prosthetic leakage, recurrent disease must be ruled out as an underlying etiology. Ultimately, when conservative management is unsuccessful, some patients may require surgical closure of the tracheoesophageal fistula tract. The complexity of this operation depends heavily on prior treatment and the *peri*-stomal tissue quality. While some authors describe success with simple tracheoesophageal tract ligation, in patients with significant radiation change a vascularized tissue reconstruction is required which may include both esophageal and posterior tracheal wall lining [103–105].

## Future directions in laryngeal rehabilitation

Despite the success of vascularized pharyngeal reconstruction and development of tracheoesophageal voice protheses to recover speech and deglutition for patients requiring total laryngectomy, full laryngeal rehabilitation – attaining speech, swallowing, and breathing without the need for a tracheostoma – remains an unsolved and complex technical challenge. The human larynx achieves an immensely difficult task with elegant simplicity. Recreating these functions in the laryngectomy patient is hindered by the loss of native laryngeal sensation and movement coupled with the toxic effects of preoperative or adjuvant radiotherapy.

There are two general approaches to recreate full laryngeal function: separation of tracheal and pharyngeal tracts or creation of a neoglottis. Tract separation requires tunneling an airway conduit from the tracheal stump to the nasopharynx which, if successful, would allow nasal breathing without a tracheostoma and swallowing without risk of aspiration. While such an endeavor has been successfully performed in a canine model using a jejunal graft and silicone stent, tract separation in humans is ultimately limited by the difficulties of long-segment tracheal replacement required to reach the nasopharynx and the challenges of recreating speech with this reconstructive paradigm [106,107].

The second approach, creation of a neoglottis, has been theorized and attempted in various forms for over 50 years [51]. It can be divided into three general strategies: prosthetic laryngeal replacement, laryngeal transplantation, and autologous surgical reconstruction [50].

**Fig. 6.** Tracheoesophageal prosthesis malfunction from accumulation of fungal elements (left) and biofilm formation (right).

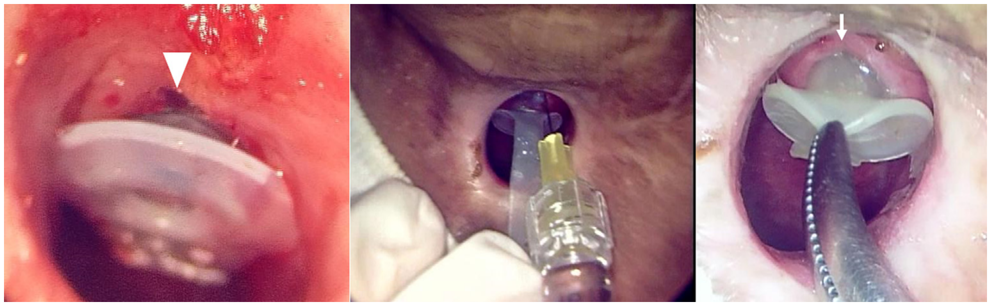

**Fig. 7.** Site of *peri*-prosthetic leakage (left, arrowhead) managed with injection of filler (center) resulting in excellent closure of the area of leakage (right, arrow).

Early experience with laryngeal prostheses in animal models were complicated by infection and obstruction [108]. Recently, authors have returned to this concept in human trials, however, and though early reports are encouraging, artificial laryngeal prostheses exposed to the upper aerodigestive tract carry a high risk of infection, migration, and erosion with potentially life-threatening consequences [109,110]. Laryngeal transplantation has been successfully performed in two human cases and has achieved excellent speech and swallowing results [111]. Reinnervation of the transplanted larynx maintains tone and not purposeful movement, however, making permanent decannulation difficult. Most importantly, this technique requires immunosuppression making it impractical after laryngectomy for malignant disease and has been shown to lead to immunosuppression-induced malignancy in the transplanted organ in long-term follow up [112]. Finally, autologous surgical reconstruction has also been attempted in humans by several authors with varying levels of success. These techniques involve a tracheopharyngeal anastomosis in various configurations and all have fundamental limitations. The recreated neoglottic aperture has been largely adynamic and often depends on preservation of laryngeal structures which are commonly removed with standard total laryngectomy such as the hyoid bone or suprahyoid epiglottis [50,108,113]. In static or minimally dynamic reconstructions, a neoglottic aperture large enough for breathing and speaking inherently increases the risk and severity of aspiration, a challenge which has ultimately precluded the wider application of these techniques outside of individual case series [114]. Even in dynamic reconstruction with partial laryngeal preservation, such as the near-total laryngectomy, without the circumferential cartilaginous support of the cricoid, patients remain tracheostomy-dependent [48].

Future work on full laryngeal rehabilitation in the laryngectomy patient must incorporate the successful aspects of these attempts and must learn from their setbacks. Development of truly dynamic surgical reconstruction is needed, with or without implantable prosthetics. Purposeful neo-glottic movement may come from innervated muscle flaps driven through phrenic nerve transfer or through implantable respiration-synced stimulation [115,116]. Sensate reconstructions may reduce aspiration. Incorporation of native pharyngeal or tracheal mucosal flaps may improve neoglottic vocal quality. These efforts, however, must bear in mind the hostile environment of the radiated upper aerodigestive tract, the risks involved in such reconstructive attempts, and must be tempered by the excellent swallowing and tracheoesophageal speech outcomes of modern laryngeal reconstruction with TEP placement.

## Conflict of interest statement

None declared.

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## References

[1] Society TAC. Key statistics for laryngeal and hypopharyngeal cancers. 2018.
[2] Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. N Engl J Med. 1991;324:1685–90.
[3] Grover S, Swisher-McClure S, Mitra N, Li J, Cohen RB, Ahn PH, et al. Total laryngectomy versus larynx preservation for T4a larynx cancer: patterns of care and survival outcomes. Int J Radiat Oncol Biol Phys 2015;92:594–601.
[4] Members NP. NCCN clinical practice guidelines in oncology: head and neck cancer. 2018.
[5] Sandulache VC, Vandelaar LJ, Skinner HD, Cata J, Hutcheson K, Fuller CD, et al. Salvage total laryngectomy after external-beam radiotherapy: a 20-year experience. Head Neck 2016;38(Suppl 1):E1962–8.
[6] Laccourreye O, Garcia D, Maldent JB, Werner A. [Evolution of laryngectomy based on a comparison of two cohorts a century apart: an illustration of the progress, difficulties and conflicts encountered in medicine]. Bull Acad Natl Med 2011;195:741–53.
[7] Ward EC, Bishop B, Frisby J, Stevens M. Swallowing outcomes following laryngectomy and pharyngolaryngectomy. Arch Otolaryngol Head Neck Surg 2002;128:181–6.
[8] Robertson SM, Yeo JC, Dunnet C, Young D, Mackenzie K. Voice, swallowing, and quality of life after total laryngectomy: results of the west of Scotland laryngectomy audit. Head Neck 2012;34:59–65.
[9] Maclean J, Cotton S, Perry A. Variation in surgical methods used for total laryngectomy in Australia. J Laryngol Otol 2008;122:728–32.
[10] Mahalingam S, Srinivasan R, Spielmann P. Quality-of-life and functional outcomes following pharyngolaryngectomy: a systematic review of literature. Clin Otolaryngol 2016;41:25–43.
[11] Gadepalli C, de Casso C, Silva S, Loughran S, Homer JJ. Functional results of pharyngo-laryngectomy and total laryngectomy: a comparison. J Laryngol Otol 2012;126:52–7.
[12] Kazi R, Prasad V, Venkitaraman R, Nutting CM, Clarke P, Rhys-Evans P, et al. Questionnaire analysis of the swallowing-related outcomes following total laryngectomy. Clin Otolaryngol 2006;31:525–30.
[13] Tan NC, Lin PY, Kuo PJ, Tsai YT, Chen YC, Nguyen KT, et al. An objective comparison regarding rate of fistula and stricture among anterolateral thigh, radial forearm, and jejunal free tissue transfers in circumferential pharyngo-esophageal reconstruction. Microsurgery 2015;35:345–9.
[14] Perez-Smith D, Wagels M, Theile DR. Jejunal free flap reconstruction of the pharyngolaryngectomy defect: 368 consecutive cases. J Plast Reconstr Aesthet Surg 2013;66:9–15.
[15] Schaefer SD, Close LG, Reisch JS. Conservation of the hypopharyngeal mucous membrane in total laryngectomy. Arch Otolaryngol Head Neck Surg 1987;113:491–5.
[16] McConnel FM, Cerenko D, Mendelsohn MS. Dysphagia after total laryngectomy. Otolaryngol Clin North Am 1988;21:721–6.
[17] Hui Y, Wei WI, Yuen PW, Lam LK, Ho WK. Primary closure of pharyngeal remnant after total laryngectomy and partial pharyngectomy: how much residual mucosa is sufficient? Laryngoscope 1996;106:490–4.
[18] Hui Y, Ma KM, Wei WI, Ho WK, Yuen PW, Lam LK, et al. Relationship between the size of neopharynx after laryngectomy and long-term swallowing function: an assessment by scintigraphy. Otolaryngol Head Neck Surg 2001;124:225–9.
[19] Maclean J, Szczesniak M, Cotton S, Cook I, Perry A. Impact of a laryngectomy and surgical closure technique on swallow biomechanics and dysphagia severity. Otolaryngol Head Neck Surg 2011;144:21–8.
[20] Deschler DG, Doherty ET, Reed CG, Hayden RE, Singer MI. Prevention of pharyngoesophageal spasm after laryngectomy with a half-muscle closure technique. Ann Otol Rhinol Laryngol 2000;109:514–8.
[21] Pauloski BR, Blom ED, Logemann JA, Hamaker RC. Functional outcome after surgery for prevention of pharyngospasms in tracheoesophageal speakers. Part II: swallow characteristics. Laryngoscope 1995;105:1104–10.
[22] Rosenthal DI, Mohamed AS, Weber RS, Garden AS, Sevak PR, Kies MS, et al. Long-term outcomes after surgical or nonsurgical initial therapy for patients with T4 squamous cell carcinoma of the larynx: a 3-decade survey. Cancer 2015;121:1608–19.
[23] Weber RS, Berkey BA, Forastiere A, Cooper J, Maor M, Goepfert H, et al. Outcome of salvage total laryngectomy following organ preservation therapy: the Radiation

Therapy Oncology Group trial 91–11. Arch Otolaryngol Head Neck Surg 2003;129:44–9.
[24] Jung TT, Adams GL. Dysphagia in laryngectomized patients. Otolaryngol Head Neck Surg 1979;1980(88):25–33.
[25] Chone CT, Spina AL, Barcellos IH, Servin HH, Crespo AN. A prospective study of long-term dysphagia following total laryngectomy. B-ENT 2011;7:103–9.
[26] Deschler DG, Blevins NH, Ellison DE. Postlaryngectomy dysphagia caused by an anterior neopharyngeal diverticulum. Otolaryngol Head Neck Surg 1996;115:167–9.
[27] van der Kamp MF, Rinkel RNPM, Eerenstein SEJ. The influence of closure technique in total laryngectomy on the development of a pseudo-diverticulum and dysphagia. Eur Arch Otorhinolaryngol 2017;274:1967–73.
[28] Howell RJ, Postma GN. Neopharyngeal diverticulum. Ear Nose Throat J 2014;93:297.
[29] Gacek RR. Management of vallecular pseudodiverticulum. Ann Otol Rhinol Laryngol 1980;89:201–3.
[30] Sweeny L, Golden JB, White HN, Magnuson JS, Carroll WR, Rosenthal EL. Incidence and outcomes of stricture formation postlaryngectomy. Otolaryngol Head Neck Surg 2012;146:395–402.
[31] Harris RL, Grundy A, Odutoye T. Radiologically guided balloon dilatation of neopharyngeal strictures following total laryngectomy and pharyngolaryngectomy: 21 years' experience. J Laryngol Otol 2010;124:175–9.
[32] Annino DJ, Goguen LA. Mitomycin C for the treatment of pharyngoesophageal stricture after total laryngopharyngectomy and microvascular free tissue reconstruction. Laryngoscope 2003;113:1499–502.
[33] Zehetner J, DeMeester SR, Ayazi S, Demeester TR. Home self-dilatation for esophageal strictures. Dis Esophagus 2014;27:1–4.
[34] Urken ML, Jacobson AS, Lazarus CL. Comprehensive approach to restoration of function in patients with radiation-induced pharyngoesophageal stenosis: report of 31 patients and proposal of new classification scheme. Head Neck 2012;34:1317–28.
[35] Henderson EDD. Occurrence of flap related complications and outcomes in reconstruction of circumferential defects after total laryngopharyngectomy. Laryngoscope 2011;121:S122.
[36] Hanasono MM, Lin D, Wax MK, Rosenthal EL. Closure of laryngectomy defects in the age of chemoradiation therapy. Head Neck 2012;34:580–8.
[37] Fung K, Teknos TN, Vandenberg CD, Lyden TH, Bradford CR, Hogikyan ND, et al. Prevention of wound complications following salvage laryngectomy using free vascularized tissue. Head Neck 2007;29:425–30.
[38] Patel UA, Moore BA, Wax M, Rosenthal E, Sweeny L, Militsakh ON, et al. Impact of pharyngeal closure technique on fistula after salvage laryngectomy. JAMA Otolaryngol Head Neck Surg 2013;139:1156–62.
[39] Sayles M, Grant DG. Preventing pharyngo-cutaneous fistula in total laryngectomy: a systematic review and meta-analysis. Laryngoscope 2014;124:1150–63.
[40] Starmer HM, Quon H, Simpson M, Webster K, Tippett D, Herbert RJ, et al. Speech-language pathology care and short- and long-term outcomes of laryngeal cancer treatment in the elderly. Laryngoscope 2015;125:2756–63.
[41] Kesteloot K, Nolis I, Huygh J, Delaere P, Feenstra L. Costs and effects of tracheoesophageal speech compared with esophageal speech in laryngectomy patients. Acta Otorhinolaryngol Belg 1994;48:387–94.
[42] Sedory SE, Hamlet SL, Connor NP. Comparisons of perceptual and acoustic characteristics of tracheoesophageal and excellent esophageal speech. J Speech Hear Disord 1989;54:209–14.
[43] Schaefer SD, Johns DF. Attaining functional esophageal speech. Arch Otolaryngol 1982;108:647–9.
[44] Verkerke GJ, Thomson SL. Sound-producing voice prostheses: 150 years of research. Annu Rev Biomed Eng 2014;16:215–45.
[45] Kaye R, Tang CG, Sinclair CF. The electrolarynx: voice restoration after total laryngectomy. Med Devices (Auckl) 2017;10:133–40.
[46] Aam R. Observation sur une fistule aérienne, avec occlusion complètte de la partie inférieure du larynx, pour servir à l'histoire de la phonation. Gaz méd Paris 1841;9:583–5.
[47] C G. Über die erste durch Th. Billroth am ausgeführte Kehlkopf-Extirpation und die Anwendung eines künstlichen Kehlkopfes. Arch Klin Chir Berlin. 1874;17:343–56.
[48] Pearson BW, Woods RD, Hartman DE. Extended hemilaryngectomy for T3 glottic carcinoma with preservation of speech and swallowing. Laryngoscope 1980;90:1950–61.
[49] Amatsu M. A new one-stage surgical technique for postlaryngectomy speech. Arch Otorhinolaryngol 1978;220:149–52.
[50] Arslan M, Serafini I. Restoration of laryngeal functions after total laryngectomy. Report on the first 25 cases. Laryngoscope 1972;82:1349–60.
[51] Ogura JH, Shumrick DS, Lapidot A. Some observations on experimental laryngeal substitution in laryngectomized dogs. Trans Am Laryngol Assoc 1962;83:77–97.
[52] Singer MI, Blom ED. An endoscopic technique for restoration of voice after laryngectomy. Ann Otol Rhinol Laryngol 1980;89:529–33.
[53] van Sluis KE, van der Molen L, van Son RJJH, Hilgers FJM, Bhairosing PA, van den Brekel MWM. Objective and subjective voice outcomes after total laryngectomy: a systematic review. Eur Arch Otorhinolaryngol 2018;275:11–26.
[54] Gitomer SA, Hutcheson KA, Christianson BL, Samuelson MB, Barringer DA, Roberts DB, et al. Influence of timing, radiation, and reconstruction on complications and speech outcomes with tracheoesophageal puncture. Head Neck 2016;38:1765–71.
[55] Hutcheson KA, Lewin JS, Sturgis EM, Risser J. Outcomes and adverse events of enlarged tracheoesophageal puncture after total laryngectomy. Laryngoscope 2011;121:1455–61.
[56] Andrews JC, Mickel RA, Hanson DG, Monahan GP, Ward PH. Major complications following tracheoesophageal puncture for voice rehabilitation. Laryngoscope 1987;97:562–7.
[57] Glazer TA, Meraj T, Lyden TH, Spector ME. In-office secondary tracheoesophageal puncture with immediate prosthesis placement. Otolaryngol Head Neck Surg 2016;155:360–3.
[58] Sharma RK, Rogers M, Thind J, Mabley AT. Technique for secondary tracheo-oesophageal puncture in difficult necks. J Laryngol Otol 2003;117:718–9.
[59] Gress CD. Preoperative evaluation for tracheoesophageal voice restoration. Otolaryngol Clin North Am 2004;37:519–30.
[60] Pou AM. Tracheoesophageal voice restoration with total laryngectomy. Otolaryngol Clin North Am 2004;37:531–45.
[61] Bozec A, Poissonnet G, Chamorey E, Demard F, Santini J, Peyrade F, et al. Results of vocal rehabilitation using tracheoesophageal voice prosthesis after total laryngectomy and their predictive factors. Eur Arch Otorhinolaryngol 2010;267:751–8.
[62] Baugh RF, Lewin JS, Baker SR. Vocal rehabilitation of tracheoesophageal speech failures. Head Neck 1990;12:69–73.
[63] Maves MD, Lingeman RE. Primary vocal rehabilitation using the Blom-Singer and Panje voice prostheses. Ann Otol Rhinol Laryngol 1982;91:458–60.
[64] Deschler DG, Bunting GW, Lin DT, Emerick K, Rocco J. Evaluation of voice prosthesis placement at the time of primary tracheoesophageal puncture with total laryngectomy. Laryngoscope 2009;119:1353–7.
[65] Chone CT, Gripp FM, Spina AL, Crespo AN. Primary versus secondary tracheoesophageal puncture for speech rehabilitation in total laryngectomy: long-term results with indwelling voice prosthesis. Otolaryngol Head Neck Surg 2005;133:89–93.
[66] Cheng E, Ho M, Ganz C, Shaha A, Boyle JO, Singh B, et al. Outcomes of primary and secondary tracheoesophageal puncture: a 16-year retrospective analysis. Ear Nose Throat J 2006;85(262):4–7.
[67] Sethi RKV, Deschler DG. National trends in primary tracheoesophageal puncture after total laryngectomy. Laryngoscope 2017.
[68] Chakravarty PD, McMurran AEL, Banigo A, Shakeel M, Ah-See KW. Primary versus secondary tracheoesophageal puncture: systematic review and meta-analysis. J Laryngol Otol. 2018;132:14–21.
[69] Emerick KS, Tomycz L, Bradford CR, Lyden TH, Chepeha DB, Wolf GT, et al. Primary versus secondary tracheoesophageal puncture in salvage total laryngectomy following chemoradiation. Otolaryngol Head Neck Surg 2009;140:386–90.
[70] Parikh SR, Irish JC, Curran AJ, Gullane PJ, Brown DH, Rotstein LE. Pharyngocutaneous fistulae in laryngectomy patients: the Toronto Hospital experience. J Otolaryngol 1998;27:136–40.
[71] Trudeau MD, Schuller DE, Hall DA. The effects of radiation on tracheoesophageal puncture. A retrospective study. Arch Otolaryngol Head Neck Surg 1989;115:1116–7.
[72] Divi V, Lin DT, Emerick K, Rocco J, Deschler DG. Primary TEP placement in patients with laryngopharyngeal free tissue reconstruction and salivary bypass tube placement. Otolaryngol Head Neck Surg 2011;144:474–6.
[73] Sethi RK, Kozin ED, Lam AC, Emerick KS, Deschler DG. Primary tracheoesophageal puncture with supraclavicular artery island flap after total laryngectomy or laryngopharyngectomy. Otolaryngol Head Neck Surg 2014;151:421–3.
[74] Silverman AH, Black MJ. Efficacy of primary tracheoesophageal puncture in laryngectomy rehabilitation. J Otolaryngol 1994;23:370–7.
[75] Pazardzhikliev DD, Yovchev IP. Influence of age on pharyngoesophageal spasm rates in laryngectomees. Folia Med (Plovdiv) 2007;49:42–5.
[76] Henley J, Souliere C. Tracheoesophageal speech failure in the laryngectomee: the role of constrictor myotomy. Laryngoscope 1986;96:1016–20.
[77] Singer MI, Blom ED. Selective myotomy for voice restoration after total laryngectomy. Arch Otolaryngol 1981;107:670–3.
[78] Baugh RF, Baker SR, Lewin JS. Surgical treatment of pharyngoesophageal spasm. Laryngoscope 1988;98:1124–6.
[79] Ikiz AO, Uça M, Güneri EA, Erdağ TK, Sütay S. Pharyngocutaneous fistula and total laryngectomy: possible predisposing factors, with emphasis on pharyngeal myotomy. J Laryngol Otol 2000;114:768–71.
[80] Singer MI, Blom ED, Hamaker RC. Pharyngeal plexus neurectomy for alaryngeal speech rehabilitation. Laryngoscope 1986;96:50–4.
[81] Bayles SW, Deschler DG. Operative prevention and management of voice-limiting pharyngoesophageal spasm. Otolaryngol Clin North Am 2004;37:547–58.
[82] Blom ED, Pauloski BR, Hamaker RC. Functional outcome after surgery for prevention of pharyngospasms in tracheoesophageal speakers. Part I: speech characteristics. Laryngoscope 1995;105:1093–103.
[83] Wang CP, Tseng TC, Lee RC, Chang SY. The techniques of nonmuscular closure of hypopharyngeal defect following total laryngectomy: the assessment of complication and pharyngoesophageal segment. J Laryngol Otol 1997;111:1060–3.
[84] Clevens RA, Esclamado RM, Hartshorn DO, Lewin JS. Voice rehabilitation after total laryngectomy and tracheoesophageal puncture using nonmuscle closure. Ann Otol Rhinol Laryngol 1993;102:792–6.
[85] Crary MA, Glowasky AL. Using botulinum toxin A to improve speech and swallowing function following total laryngectomy. Arch Otolaryngol Head Neck Surg 1996;122:760–3.
[86] Hoffman HT, Fischer H, VanDenmark D, Peterson KL, McCulloch TM, Karnell LH, et al. Botulinum neurotoxin injection after total laryngectomy. Head Neck 1997;19:92–7.
[87] Terrell JE, Lewin JS, Esclamado R. Botulinum toxin injection for postlaryngectomy tracheoesophageal speech failure. Otolaryngol Head Neck Surg 1995;113:788–91.
[88] Hamaker RC, Blom ED. Botulinum neurotoxin for pharyngeal constrictor muscle spasm in tracheoesophageal voice restoration. Laryngoscope 2003;113:1479–82.

[89] Chao SS, Graham SM, Hoffman HT. Management of pharyngoesophageal spasm with Botox. Otolaryngol Clin North Am 2004;37:559–66.
[90] Deschler DG, Doherty ET, Reed CG, Singer MI. Quantitative and qualitative analysis of tracheoesophageal voice after pectoralis major flap reconstruction of the neopharynx. Otolaryngol Head Neck Surg 1998;118:771–6.
[91] Deschler DG, Doherty ET, Reed CG, Anthony JP, Singer MI. Tracheoesophageal voice following tubed free radial forearm flap reconstruction of the neopharynx. Ann Otol Rhinol Laryngol 1994;103:929–36.
[92] Deschler DG, Herr MW, Kmiecik JR, Sethi R, Bunting G. Tracheoesophageal voice after total laryngopharyngectomy reconstruction: Jejunum versus radial forearm free flap. Laryngoscope 2015;125:2715–21.
[93] Revenaugh PC, Knott PD, Alam DS, Kmiecik J, Fritz MA. Voice outcomes following reconstruction of laryngopharyngectomy defects using the radial forearm free flap and the anterolateral thigh free flap. Laryngoscope 2014;124:397–400.
[94] Hutcheson KA, Sturgis EM, Lewin JS. Early risk factors for enlargement of the tracheoesophageal puncture after total laryngectomy: nodal metastasis and extent of surgery. Arch Otolaryngol Head Neck Surg 2012;138:833–9.
[95] Yu P, Hanasono MM, Skoracki RJ, Baumann DP, Lewin JS, Weber RS, et al. Pharyngoesophageal reconstruction with the anterolateral thigh flap after total laryngopharyngectomy. Cancer 2010;116:1718–24.
[96] Sinclair CF, Rosenthal EL, McColloch NL, Magnuson JS, Desmond RA, Peters GE, et al. Primary versus delayed tracheoesophageal puncture for laryngopharyngectomy with free flap reconstruction. Laryngoscope 2011;121:1436–40.
[97] Noel D, Fink DS, Kunduk M, Schexnaildre MA, DiLeo M, McWhorter AJ. Secondary tracheoesophageal puncture using transnasal esophagoscopy in gastric pull-up reconstruction after total laryngopharyngoesophagectomy. Head Neck 2016;38:E61–3.
[98] Bleach N, Perry A, Cheesman A. Surgical voice restoration with the Blom-Singer prosthesis following laryngopharyngoesophagectomy and pharyngogastric anastomosis. Ann Otol Rhinol Laryngol 1991;100:142–7.
[99] Lewin JS, Baumgart LM, Barrow MP, Hutcheson KA. Device life of the tracheoesophageal voice prosthesis revisited. JAMA Otolaryngol Head Neck Surg 2017;143:65–71.
[100] Laccourreye O, Ménard M, Crevier-Buchman L, Couloigner V, Brasnu D. In situ lifetime, causes for replacement, and complications of the Provox voice prosthesis. Laryngoscope 1997;107:527–30.
[101] Tjoa T, Bunting G, Deschler DG. Injectable soft-tissue augmentation for the treatment of tracheoesophageal puncture enlargement. JAMA Otolaryngol Head Neck Surg 2018;144:383–4.
[102] Jacobs K, Delaere PR, Vander Poorten VL. Submucosal purse-string suture as a treatment of leakage around the indwelling voice prosthesis. Head Neck 2008;30:485–91.
[103] Mobashir MK, Basha WM, Mohamed AE, Anany AM. Management of persistent tracheoesophageal puncture. Eur Arch Otorhinolaryngol 2014;271:379–83.
[104] Hosal SA, Myers EN. How I do it: closure of tracheoesophageal puncture site. Head Neck 2001;23:214–6.
[105] Delaere PR, Delsupehe KG. Closure of persistent tracheoesophageal fistulas after removal of the voice prosthesis. Laryngoscope 1994;104:494–6.
[106] Hagen R, Schwab B, Marten S. Nasotracheal airway-oropharyngeal alimentary canal: a microvascular technique for reconstruction of the upper airway after total laryngectomy. Ann Otol Rhinol Laryngol 1995;104:317–22.
[107] Udelsman B, Mathisen DJ, Ott HC. A reassessment of tracheal substitutes-a systematic review. Ann Cardiothorac Surg 2018;7:175–82.
[108] Ogura JH, Shumrick DA, Lapidot A. Some observations on experimental laryngeal substitution in laryngectomized dogs. Ann Otol Rhinol Laryngol 1962;71:532–50.
[109] Debry C, Vrana NE, Dupret-Bories A. Implantation of an artificial larynx after total laryngectomy. N Engl J Med 2017;376:97–8.
[110] D'Ascanio L, Piazza F. More on implantation of an artificial larynx after total laryngectomy. N Engl J Med 2017;376:e29.
[111] Strome M, Stein J, Esclamado R, Hicks D, Lorenz RR, Braun W, et al. Laryngeal transplantation and 40-month follow-up. N Engl J Med 2001;344:1676–9.
[112] Lorenz RR, Strome M. Total laryngeal transplant explanted: 14 years of lessons learned. Otolaryngol Head Neck Surg 2014;150:509–11.
[113] Ghosh P. Malignancy of the larynx: (experimentation on animal, construction of biologic neo-larynx and rehabilitation of the laryngectomee-20 years experience). Indian J Otolaryngol Head Neck Surg 1997;49:209–27.
[114] Li CJ, Cheng L, Wu H, Tao L, Zhou L. Neoglottis reconstruction with sternohyoid muscles on upper-tracheal orifice after laryngectomy. Eur Arch Otorhinolaryngol 2017;274:383–8.
[115] Li M, Chen S, Zheng H, Chen D, Zhu M, Wang W, et al. Reinnervation of bilateral posterior cricoarytenoid muscles using the left phrenic nerve in patients with bilateral vocal fold paralysis. PLoS One 2013;8:e77233.
[116] Woodson BT, Soose RJ, Gillespie MB, Strohl KP, Maurer JT, de Vries N, et al. Three-year outcomes of cranial nerve stimulation for obstructive sleep apnea: the STAR trial. Otolaryngol Head Neck Surg 2016;154:181–8.