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Retrospective Exploration of Botulinum Toxin Injection for Pharyngoesophageal Segment Dysfunction Post-laryngectomy

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Abstract

Objective. To assess our institution's experience with botulinum toxin A injection management of pharyngoesophageal (PE) segment dysfunction after laryngectomy in tracheoesophageal voice and swallowing restoration**.**

Study Design. A retrospective review of 43 patients who had Botox as treatment for PE dysfunction.

Setting. Tertiary academic center with fellowship-trained otolaryngologists.

Methods. Pre- and post-injection outcomes were evaluated using chart review, and the severity of symptoms was recorded based on the subjective assessment by the patient, speech language pathologists, and the treating surgeon.

Results. Forty-three patients were treated for PE dysfunction with botulinum toxin A injection. Most patients were male (n = 35, 81.4%), underwent primary cricopharnygeal myotomy (n = 36, 83.7%), and 37 (86%) had both dysphagia and speech concerns. Our injection methods included percutaneous injection by videofluoroscopy (n = 19, 44.2%), transnasal esophagoscopy (17, 40.5%), electromyography (n = 3, 7%), ultrasound (n = 1, 2.3%), or in the operating room (n = 3,7%). We found that 37 (86%) patients had subjective improvement in their symptoms, with 16 (38.1%) improving in both swallow and voice. There were no significant complications, or subjective difference in speech and swallowing outcomes by method of injection.

Conclusion. Botulinum toxin A injection appears to be safe and effective for treating difficulty with speech and swallowing due to PE dysfunction after laryngectomy. Institutions should develop standard protocols for treatment and assessment.

Keywords

botulinum toxin A, botox, laryngectomy, pharyngoesophageal segment dysfunction

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Total laryngectomy (TL) has profound and long-lasting impacts on speech and swallowing. Over the years, advancements in voice restoration techniques have been remarkable. The most widely adopted method of voice restoration is the use of a tracheoesophageal (TEP) voice prosthesis, described by Singer and Blom in 1980.[1,2] Although success rates remain high, there are still complications that can confound TEP voice and swallowing. Pharyngoesophageal (PE) segment hypertonicity and spasm is a well-recognized phenomenon, and it is reported to account for up to 79% of TE speech failures.[3-5] Likewise, some series report that PE dysfunction is responsible for 22% to 36% of dysphagia complications after laryngectomy.[6] PE dysfunction is failure of PE muscle relaxation that disrupts the physiology of swallowing and prevents adequate airflow through the pharynx, which manifests as spasmodic speech.[4] The traditional treatment modalities for PE dysfunction includes speech and swallow therapy and surgical cricopharyngeal (CP) myotomy, as dilation is usually unsuccesful.[3-5] CP myotomy is usually carried out at the time of laryngectomy and, less frequently, as a secondary procedure due to potential severe complications and financial implications.[6] At our institution CP myotomy is performed during laryngectomy, but patients may still develop PE dysfunction consistent with other institution's experience.[4] It is unknown why certain patients

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have postoperative PE dysfunction, but incomplete myotomy or muscle regeneration have been proposed.

For those patients with PE dysfunction, botulinum toxin A injection is particularly appealing, as it offers a minimally invasive, safe, and durable therapeutic option for improving speech and swallow in this population.[3,4,7-16] Techniques for the administration of injections are diverse, including those guided by videofluoroscopy, electromyography, rigid pharyngoscopy under general anesthesia, esophagogastroduodenoscopy, videostroboscopy, and ultrasound (US).[10,14-16] Evaluation metrics for success have encompassed various parameters including pre- and post-injection subjective evaluation by speech pathologists, tracheal air pressure measures, self-report measures, changes in weight, videofluoroscopy, computerized manometry, barium swallows, and videostroboscopy recordings.[3,4,14] However, it's noteworthy that existing studies have been small (range n = 1-23 patients) and have reported a single technique for injection. This study reviews our institutions' experience with botulinum toxin A injection in a cohort of patients with PE dysfunction after laryngectomy using multiple modalities of injection.

Materials and Methods

Study Overview

We conducted a retrospective study at the University of Michigan with Institutional Review Board exemption (HUM00236663) from ongoing review.

Study Setting and Participants

The University of Michigan is a multidisciplinary, tertiary, referral head-and-neck institution. We retrospectively identified patients ≥18 years of age with prior laryngectomy who underwent botulinum toxin A injection to the cricopharyngeus muscle to address post-laryngectomy dysphonia and/or dysphagia between 2000 and 2023 at our institution using *Data Direct Database*. All patients had regular 3-month evaluation of the TEP with quality maintenance and all patients included in the study had normal valve function. We excluded patients with TEP dysfunction including fungal infection, dilated punctures, valve deterioration, and occlusion by crusting or tissue. We also excluded patients with esophageal strictures.

Pharyngoesophageal Spasm (PES) Evaluation and Injection

Patients presenting with clinical symptoms of speech and/or swallowing function potentially resulting from PE dysfunction were screened initially by a specialist clinic comprising a speech and language therapist, consultant radiologist, and consultant head and neck surgeon. All patients deemed clinically likely to have PES dysfunction had further confirmation studies evaluating speech and/or swallow patient concerns with either pretreatment videofluoroscopy, transnasal endoscopy (TNE), or videofluoroscopy at the time of injection. Videofluoroscopic confirmation that showed nonyielding stenosis in the PE, esophageal dysmotility, normal results, and/or redirection of contrast was not included in the study.[3-5] A transient narrowing of the PE related to physiological activity (speech or swallowing) was considered to represent dysfunction/spasm and amenable to botox injection, consistent with prior literature.[7,9-11] Similar criteria were used for confirmation by TNE with direct visualization of the PE segment spasm with voicing and swallowing.

The methods of botulinum toxin A injection were chosen by surgeon training and comfort with the technique. It included videofluoroscopy-guided injections described by the senior author,[17] electromyography (EMG)-guided injection,[18] US-guided injection,[19,20] and TNE-guided transcutaneous injection. We are unable to find TNE-guided transcutaneous injection, only TNE with a needle injector, in the literature. For this technique, the patient is placed in the examination chair in the clinic in the upright position. Local anesthesia is assured by tetracaine spray in the nose and 4% viscous lidocaine swallow. After allowing adequate time for anesthetic effect, the flexible TNE scope is passed through the naris. The scope is passed just proximal to the gastroesophageal junction assessing the neopharynx and esophagus for strictures and/or evidence of CP muscle dystonia. The scope is then withdrawn to the level of PE dysfunction. Externally, additional local anesthetic is injected into the anterior neck skin superior to the TEP. Under direct visualization with TNE scope at the level of narrowing, a 30-Gauge needle is then advanced into the pharynx transcutaneous. Under direct visualization the CP muscle segment in dysfunction is injected with botulinum toxin A.

Assessment and Data analysis

The severity of symptoms was recorded pre- and post-injection based on subjective assessment by the patient, by our speech language pathologists, and the treating surgeon. Results were categorized as improved speech, improved swallow, improvement in both, no improvement, or worsened symptoms if 2 of the 3 subjective assessments were alike. Data was analyzed using SPSS 26. Pearsons χ^2 were conducted due to small study cohort sizes with an α level of 0.05.

Results

Patients

A total of 43 patients who had undergone a TL were evaluated for PE dysfunction that interfered with swallowing and/or voicing. The average age was 65 (±9) and most were male (81%) (**Table 1**). Seven (16%) of the patients had free flap reconstruction during surgery and 27 (63%) had primary TEP placement. Thirty-four (79%)

Table 1. Demographics and Clinical Characteristics of Patients (n = 43)

Age, y	Mean (SD)	65 (±9)
Sex	Male	35 (81)
	Female	8 (19)
Ethnicity	Black	2 (5)
	Caucasian	39 (91)
	Other	2 (5)
Tobacco use	Never	3 (7)
	Former	25 (58)
	Current	2 (5)
	Undocumented	13 (30)
Alcohol use	No	11 (26)
	Yes	17 (40)
	Undocumented	15 (35)
BMI	Mean (SD)	24 (±5)

N (%) or mean (±standard deviation).
Abbreviation: BMI, body mass index.

Table 2. Clinical Assessment and Characteristics Relevant to Botulinum A Toxin Injection

CP myotomy during laryngectomy performed	
No	4 (9)
Yes	36 (84)
Symptoms	
Voice concerns	4 (9)
Dysphagia	2 (5)
Both	37 (86)
Initial testing	
Videofluoroscopy	40 (93)
Transnasal endoscopy only	1 (2)
Fluoroscopy only	2 (5)
Type of voice	
TEP	43 (100)
Other	0 (0)
Time to botox from surgery	
Mean, y	4.1 ± 6.0
Botox amount	
Mean, units	61.15 ± (19 units)

N (%) or mean ± standard deviation.
Abbreviations: CP, cricopharyngeal; TEP, tracheoesophageal prosthesis.

patients had pre-laryngectomy radiation therapy and 4 (9%) had pre- and post-laryngectomy radiation therapy. Only 5 (12%) patients did not receive any radiation therapy. Thirty-eight (88%) of the patients had been evaluated by SLP and undergone extensive voice therapy. CP myotomy was documented as performed in 36 (84%) patients at the same time as their laryngectomy (**Table 2**). The mean time (SD) from laryngectomy to botulinum toxin A injection was 4 ± 6 years. Prior to the botulinum toxin A injection, 4% had dysphagia only, 9% of patients had voice concerns only, and 86% had both dysphagia and speech concerns. All used a TEP voice, consistent with our typical practice for speech rehabilitation after laryngectomy.[18]

PE Dysfunction Evaluation and Injection Technique

All patients in the cohort reported symptoms of dysphagia and/or voice concerns and were then further evaluated by either videofluoroscopy (n = 40, 93%), direct visualization on TNE (n = 1, 2%), or taken to the fluoroscopy suite for same time evaluation and planned injection (n = 2, 5%). Videofluoroscopy studies were dictated by radiology and SLP, patients were deemed to have PE dysfunction if there was cricopharyngeal prominence and failed dynamic relaxation on swallowing and voice testing (**Figure 1**).

The methods of botulinum toxin A injection included videofluoroscopy-guided injections for 19 (44%) patients (**Figure 2**), TNE-guided injection for 17 (41%) of patients, EMG guided-injection for 3 (7%) patients, US-guided injection for 1 (2%) of patients, and 3 (7%) performed in the operating room (**Figure 3**). The mean amount of botulinum toxin A injected at the initial visit was 61 ± 19 units, and subsequent doses were titrated for dose-dependent benefits. Subsequent injections of botulinum toxin were requested by 22 (51%) patients for return of dysphagia symptoms or difficulty in voice production.

Outcomes

Primary determination of benefit was determined by agreement of 2 out of 3 subjective evaluations by the patient, SLP, and provider. Of the 42 patients, 1 was lost to follow-up, 37 (86%) had subjective improvement in their symptoms (**Figure 4**). Of these, 16 (38%) patients had improvement in their swallow and in their voice. Additionally, 12 (29%) had improvement only in their swallow. Of these patients with improvement in their swallow, 2 noted weakened voices following injection. Furthermore, 8 (19%) patients only had improvement in their voice but not in their swallow. Of these, 5 patients had voice concerns only and 3 patients did endorse dysphagia, but it was unaffected by the botulinum A toxin injection. Finally, 5 (12%) patients did not have any benefit or effect on their swallow or speech and 1 (2%) had worsening of their swallow and voice following injection. Eight patients (19%) required only 1 injection for durable improvement. The average was 2 injections (range 1-4), which improved 25 (60%) patients' symptoms. We found only 1 patient (2.3%) refused a second injection after failure in improvement. The other 4 patients with failure in improvement stopped injections after 2, 3, 4, and finally 5 injections. The average duration of response was 8.1 months. Subjective comparison among injection techniques demonstrated no notable difference but was likely under-powered (**Table 3**). When comparing only videofluoroscopy-guided versus TNE, we still did not find any significant differences. We

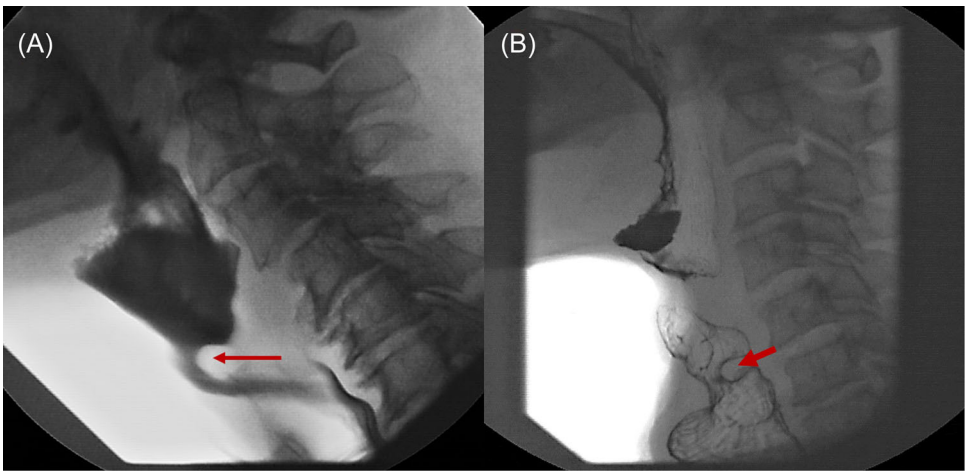

Figure 1. (A) Videofluoroscopy study demonstrating pharyngoesophageal segment spasm with liquids (red arrow). (B) Videofluoroscopy study demonstrating pharyngoesophageal segment spasm with voicing (red arrow).

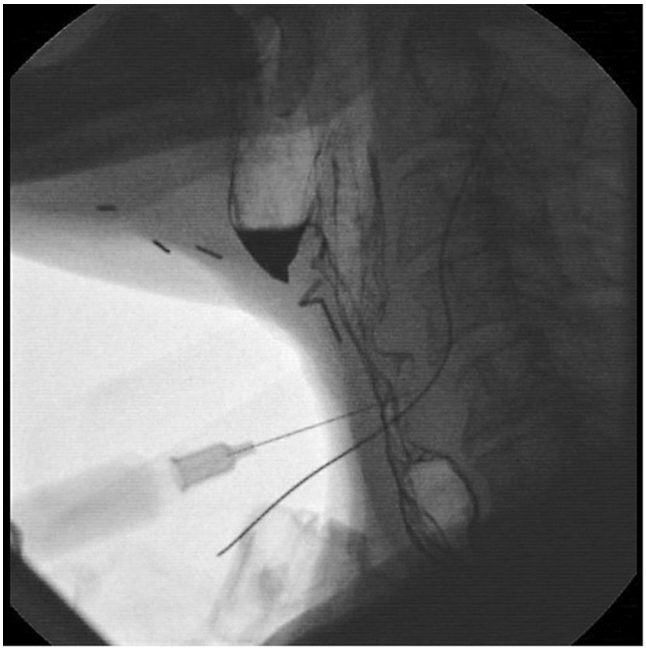

Figure 2. Video fluoroscopic guidance of pharyngoesophageal segment spasm botulinum toxin A injection.

found an average weight gain of 4 ± 5 lbs at clinic appointments 12 months after the injection.

Discussion

For those that fail speech and swallow therapy, in clinic botulinum toxin A injection stands out as an accessible, affordable, and well-tolerated option for patients with PE dysfunction following laryngectomy.[1,4,15] Given the limited literature in this area, our retrospective cohort study aims to provide insights into the potential uses, techniques, and outcomes associated with botulinum toxin injection for PE dysfunction. Our cohort of 43 patients is one of the largest in the literature, and subjective improvement of symptoms was 86% after Botox injection. Eight patients (19%) required only 1 injection, but the average was 2 injections (range 1-4), which improved 25 (60%) patients' symptoms. Speech quality improved in 18%, swallowing in 29%, and both speech and swallow in 38% of patients. We also demonstrate success with multiple clinic modalities for injection that may save operating room time and cost. Our experience and reviewing of the literature demonstrates significant limitations in objective measures and protocols to treat this debilitating problem. Validated assessment protocols and clinical trials should be performed with the goal of improving quality of life for these patients.

There is a myriad of options for improving speech and swallowing after laryngectomy. Dilation is usually more successful for relieving dysphagia due to stricture. Pharyngeal neurectomy and cricopharyngeal myotomy have good success rates, but involve an open procedure and a risk of pharyngocutaneous fistula. Given its minimally invasive, fairly inexpensive, and reversible nature, chemical denervation has become a great option. Similar success rates to ours can be found in the literature, though most evaluate either swallowing or voice outcomes. However, there are considerable differences in the applied diagnostic studies, injection techniques, and assessment of outcomes. Only 2 studies have evaluated a cohort of more than 11 patients. Hamaker and Blom,[18] reviewed 62 laryngectomized patients who had been treated with EMG-guided botox and could demonstrate an improvement in voice quality in 89% of the cases. Lewin et al,[11] reported a success rate of 65% after the first injection, which increased to 87% with 1 or 2 more injections. Both studies used EMG-guided injections, but others have reported techniques using US, videofluoroscopy, or TNE. They all seem to have evidence of efficacy, mostly anecdotal, but have never been compared directly.

At our institution we frequently perform transcutaneous botulinum toxin A injection in the fluoroscopy

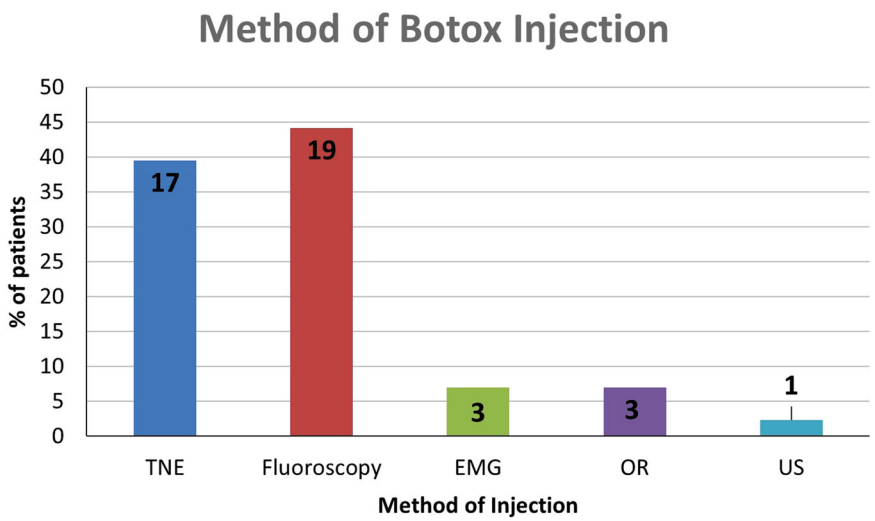

Figure 3. Description of the method of botulinum toxin A injection employed out of 43 patients. EMG, electromyography; OR, operating room; TNE, transnasal endoscopy; US, ultrasound.

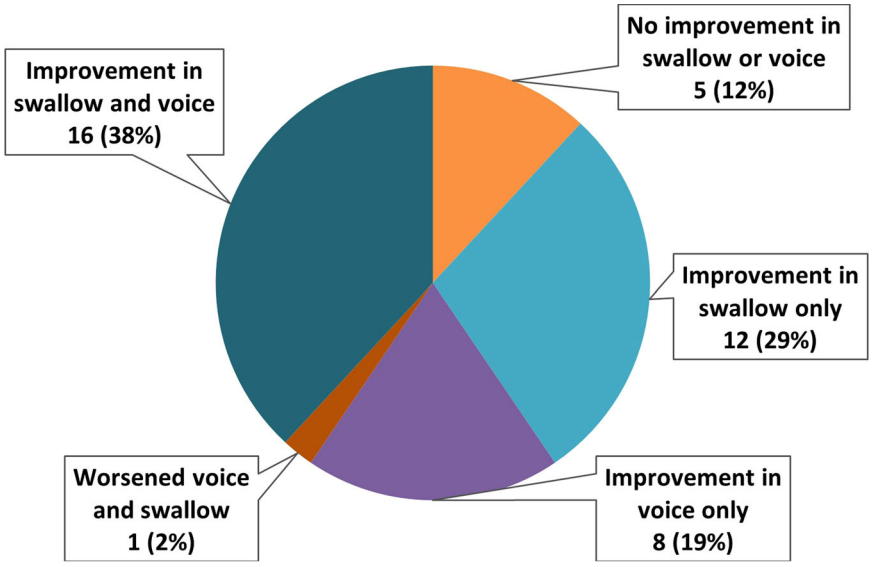

Figure 4. Subjective effect of botulinum toxin A injection on dysphagia and/or dysphonia.

suite which allows for simultaneous diagnosis. This technique has been previously described by the senior author.[17] The transcutaneous videofluoroscopic-guided injection method provides precision in delineating the specific CP muscle segment to target with the needle. Furthermore, the multi-dimensional views facilitated slight adjustments in the needle trajectory, enabling multiple injections through the same skin puncture site.[17] However, it requires greater time, resources, and cost to perform them within a radiology suite. In contrast, EMG-guided injections[18] and US-guided injections provide significantly less accuracy, but can be conveniently performed in a clinic setting, likely making them less demanding in terms of time and personnel resources.[19,20]

Our team also performs frequent transcutaneous TNE-guided injections. TNE-guided injections introduce a method that offers the advantage of being performed within a clinical setting while maintaining a precise anatomical view of the dynamic dysfunction during injection. Our study subjectively compared the techniques and found the outcomes to be similar but is not powered for definitive conclusions to be made.

The primary limitation of this study was that our outcome is a subjective report of improvement. Notably, there is no standardized measure for fluency of TEP speech or scoring of dysphagia in post-laryngectomy patients. While some studies have used objective measures, such as PES pressures, voice recordings, or pre- and post-injection imaging, these are small cohort studies and there is no standard of practice.[4,9,14] In our study, measure of success of the injection was based on the subjective evaluation of the patient, speech and language pathologist, and the surgeon. Some scoring systems have been considered in other studies. The University of

Table 3. Summary of the Effect of Different Methods of Guided Botulinum Toxin A Injection on Swallowing and Voicing

Summary of effect, total	TNE-guided botox injections, N = 17 (%)	Fluoroscopy-guided botox injections, N = 18 (%)	Electromagnetic guidance, N = 3 (%)	Operating room guidance, N = 3 (%)	Ultrasound guidance, N = 1 (%)	Pearson χ^2 value
Improvement in swallow and voice	6 (35)	7 (29)	2 (67)	0	1 (100%)	0.33
Improvement in swallow only	5 (29)	5 (28)	0	2 (67)	0	0.44
Improvement in voice only	3 (18)	5 (28)	0	0	0	0.63
No improvement in swallow or voice	3 (18)	0	1 (33)	1 (33)	0	0.22
Worsened voice and swallow	0	1 (6)	0	0	0	1.00

Abbreviation: TNE, transnasal endoscopy.

Washington Quality of Life questionnaire,[21] Voice Handicap Index-30,[22] and the MD Anderson Dysphagia Inventory[23] could be utilized. These questionnaires can assess different issues influencing patient-perceived benefit. Each questionnaire has been validated for use in the context of surgery of the head and neck and is completed by the patient to avoid clinician bias.[4] However, these questionnaires are not validated for PE dysfunction and include questions targeted at aspiration which are not applicable to laryngectomy patients. Unfortunately, there is no good alternative at present and the authors hope that a specific tool with good psychometric properties for this group will be developed in the future. Another limitation of our study was that due to collection of data via retrospective chart review, many aspects of the patient course, symptoms, and treatments were not consistently described. Furthermore, most patient charts did not adequately or consistently describe objective measures such as opening pressures on fluoroscopy. Additionally, follow-up was inconsistent and therefore assessing ideal dosing of botulinum injections and frequency of injections may be inaccurate. Furthermore, this study selected patients who had undergone botulinum toxin injection and therefore did not include a comparison group or assess patients who declined injections, creating selection bias. Finally, there are several potential confounding variables that could account for patients' symptoms. First, it's worth noting that a majority of the patients in this study had undergone radiation therapy prior to their botulinum toxin injection. Consequently, radiation fibrosis likely contributed to dysfunction, although we did not specifically assess its impact in this study. In future investigations, conducting comparisons between cohorts with and without radiation therapy could be beneficial. Second, reflux is frequently observed following laryngectomy and is a documented contributor of valve failure.[24,25] While we did not find evidence of worsening reflux in our chart review, it could be an important variable to measure and treat in future studies.

For next steps, conducting a prospective observational study using objective measures would offer valuable insights into further comparing the impact of botulinum toxin A injection. Intergroup comparisons between different injection techniques would offer new data that could significantly influence clinical practices. Additionally, conducting a cost-comparison of the various techniques may provide further incentive for surgeons to preferentially select one method over another.

Conclusion

In conclusion, PE dysfunction represents a significant complication following laryngectomy, often resulting in TEP speech and swallowing failures. Through a retrospective chart review of our institution's experience with botulinum toxin A injection, we demonstrate its potential as an efficacious treatment option for addressing this

challenge. The limited objective data available at our institution and within the literature, prevents definitive conclusions on best practices. Nevertheless, our study provides a framework upon which institutions can self-explore and develop standard treatment protocols and methods of assessment in order to identify which options are most effective and affordable. Further research should focus on the gaps within the literature on the diagnosis, treatment, and assessment for botulinum toxin injection treatment of PE dysfunction.

Author Contributions

Ruby J. Kazemi, concept and design of the study, acquisition, analysis, and interpretation of data, drafting of the manuscript; **Andrew D.P. Prince**, concept and design of the study, acquisition, analysis, and interpretation of data, drafting of the manuscript; **Keith A. Casper**, critical revision of the manuscript for important intellectual content; **Matthew E. Spector**, critical revision of the manuscript for important intellectual content; **Joshua D. Smith**, concept and design of the study, critical revision of the manuscript for important intellectual content; **Mark E.P. Prince**, concept and design of the study, critical revision of the manuscript for important intellectual content.

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