Biomechanics of Pharyngeal Deglutitive Function following Total Laryngectomy

Teng Zhang, MEng1,2, Michal Szczesniak, PhD1,2, Julia Maclean, PhD3, Paul Bertrand, PhD4, Peter I. Wu, MD2, Taher Omari, PhD5, and Ian J. Cook, MD, PhD1,2

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Abstract

Objective. Postlaryngectomy, pharyngeal weakness, and pharyngoesophageal junction (PEJ) restriction are the candidate mechanisms of dysphagia. The aims were, in laryngectomees, whether (1) hypopharyngeal propulsion is reduced and/or PEJ resistance is increased, (2) dilatation improves dysphagia, and (3) whether symptomatic improvement correlates with reduced PEJ resistance.

Design. Multidisciplinary cross-sectional study.

Setting. Tertiary academic hospital.

Subjects and Methods. Swallow biomechanics were assessed in 30 laryngectomees. Patients were stratified into severe dysphagia (Sydney Swallow Questionnaire >500) and mild/nil dysphagia (Sydney Swallow Questionnaire ≤500). Average hypopharyngeal peak (contractile) pressure (hPP) and hypopharyngeal intrabolus pressure (hIBP) were measured from high-resolution manometry with concurrent videofluoroscopy based on barium swallows (2.5 and 10 mL). In consecutive 5 patients, measurements were repeated after dilatation.

Results. Dysphagia was reported by 87%, and 57% had severe and 43% had mild/nil dysphagia. hIBP increased with larger bolus volumes (P < .0001), while hPP stayed stable and PEJ diameter plateaued at 9 mm. Laryngectomees had lower hPP (110 ± 14 vs 170 ± 15 mm Hg; P = .0162) and higher hIBP (29 ± 5 vs 6 ± 5 mm Hg; P = .156) than controls. There were no differences in hPP between patient groups. However, hIBP was higher in severe than in mild/nil dysphagia (41 ± 10 vs 13 ± 3 mm Hg; P = .02). Predilation hIBP (R² = 0.97) and its decrement postdilatation (R² = 0.98) well predicted symptomatic improvement.

Conclusions. PEJ resistance correlates better with dysphagia severity than peak pharyngeal pressure and is more sensitive to bolus sizes than PEJ diameter. Both baseline PEJ resistance and its decrement following dilatation are strong predictors of treatment outcome. PEJ resistance is vital to detect, as it is reversible and can predict the response to dilatation regimens.

Keywords

laryngectomy, pharynx, deglutition, dysphagia, hypopharyngeal intrabolus pressure, hypopharyngeal peak contractile pressure, biomechanics, motility, high-resolution manometry, videofluoroscopy, dilatation, resistance

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Respiratory, phonatory, and deglutitive functions of the laryngectomees are dramatically altered, leading to significant morbidity. Total laryngectomy involves surgical excision of the larynx and epiglottis, as well as strap muscles, thyroid and cricoid cartilage, hyoid bone, and up to 2 proximal tracheal rings. The precise nature and extent of the surgery and postresection pharyngeal closure vary markedly depending on tumor extent and surgeon preference. Wherever possible, adequate pharyngeal mucosa is preserved to ensure satisfactory postoperative phonation and deglutition functions.

Dysphagia following laryngectomy is common, with the reported prevalence varying widely from 17% to 72%. The cause of dysphagia is multifactorial; while tumor occurrence can be a cause of dysphagia, impaired pharyngeal propulsion can result from surgical damage to the pharyngeal muscles, compounded by adjuvant radiation-related neuromuscular dysfunction. Contributory causes of increased outflow resistance across the pharyngoesophageal junction (PEJ) include reduced caliber of the PEJ resulting from removal of the cricoid cartilage,

1Department of Gastroenterology and Hepatology, St George Hospital, Sydney, Australia
2School of Medicine, University of New South Wales, Sydney, Australia
3Department of Speech Pathology, St George Hospital, Sydney, Australia
4School of Medical Science, University of RMIT, Melbourne, Australia
5School of Medical Science, Flinders University, Adelaide, Australia

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Corresponding Author:
Teng Zhang, MEng, Department Gastroenterology and Hepatology, Level 1, Burt Wing, St George Hospital, Gray St, Kogarah, 2217, Australia.
Email: teng.zhang@unsw.edu.au
as well as loss of extrinsic hyolaryngeal tractional forces on the upper esophageal sphincter.\textsuperscript{13-16} Additionally, adjuvant radiotherapy, administered in up to 84\% of late-stage laryngeal cancers patients, can create fibrosing PEJ strictures.\textsuperscript{17,19}

The biomechanics of deglutition following laryngectomy has received little attention. From early manometric studies in laryngectomees, pharyngeal neuromyopathic dysfunction results in reduction of the pharyngeal contractile pressure.\textsuperscript{13,14,20-23} and that bolus transition time during the pharyngeal deglutitive phase is increased.\textsuperscript{23,24} However, the clinical relevance of these manometric and temporal findings remains unclear, as none related these parameters specifically to the clinical status of the patients. In addition, other crucial pharyngeal manometric parameters, such as the measurement of resistance to bolus flow, were not studied, nor have there been attempts to correlate manometric measures with the treatment outcomes.

The aim of this study was to characterize the biomechanics of pharyngeal deglutitive dysfunction in laryngectomees with dysphagia, with a view to gain insights into possible predictors of symptom severity and treatment outcome following dilatation. Our specific aims were to determine (1) whether hypopharyngeal prolusion is reduced and/or PEJ resistance is increased and what the relative importance of these 2 biomechanical parameters is and (2) whether symptomatic improvement following dilatation correlates with reduction in resistance across the PEJ and whether it can be predicted by predilatation biomechanical measures.

\textbf{Methods}

\textbf{Patients}

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

Patients were eligible for study if they had had total laryngectomy at least 12 months prior. Patients with or without dysphagia symptoms were recruited through a variety of sources, including the departments of gastroenterology, speech pathology, and radiation oncology as well as the New South Wales laryngectomy association. Patients were excluded from study if they had any history of local tumor recurrence or any neurologic disorder potentially associated with dysphagia (eg, prior cerebrovascular accident, Parkinson’s disease, myopathy) or known esophageal pathology causing dysphagia (eg, esophageal stricture, malignancy).

\textbf{Dysphagia Severity}

Dysphagia severity was assessed with the Sydney Swallow Questionnaire (SSQ),\textsuperscript{25} a validated self-reporting swallowing assessment tool for oral-pharyngeal dysphagia that has also been validated in a head and neck cancer population.\textsuperscript{26} SSQ scores range from 0 to 1700, with an upper limit of normal being 234.\textsuperscript{27} Patients were stratified into 2 groups: severe dysphagia (SSQ score >500) and mild or nil dysphagia (SSQ score ≤500). The chosen threshold score of 500 was based on clinical experience in that the majority of patients with self-reported moderate to severe dysphagia have SSQ scores >500.

\textbf{Biomechanical Measurements}

Pharyngeal propulsion and PEJ resistance were assessed with high-resolution manometry (HRM) combined with concurrent video fluoroscopy as described previously.\textsuperscript{28,29} Briefly, with participants seated upright, the manometry catheter (Unisensor USA Inc, Portsmouth, New Hampshire), with a diameter of 3.6 mm incorporating 25 solid-state pressure sensors at 1-cm spacing, was positioned transnasally to span the pharynx and the PEJ after topical nasal anesthesia (lidocaine 10\%). Videofluoroscopic cine loops were acquired (MultiDiagnost Eleva; Philips, Best, The Netherlands) and recorded concurrently with HRM via a Solar GI System (software version 8.210; MMS, Enschede, The Netherlands). Participants swallowed triplicate boluses of 2, 5, and 10 mL of EZ-HD barium (Bracco UK Limited, High Wycombe, UK).

The manometric marker of PEJ resistance was the hypopharyngeal intrabolus pressure (hIBP), defined as the pressure within the advancing bolus measured 1 cm above the upper border of the PEJ at the midpoint of bolus flow through the PEJ (Figure 1).\textsuperscript{30} The manometric measure of pharyngeal propulsion was hypopharyngeal peak (contractile) pressure (hPP),\textsuperscript{30-32} defined as the average of peak pressures recorded across a 3-cm segment above the upper margin of the PEJ at its apogee of upward excursion during the swallow\textsuperscript{33} (Figure 1). PEJ baseline tone was measured by averaging a stable 5-second epoch of HRM recording of the PEJ pressure at the end of each study. Control manometric measures were obtained from 11 healthy aged volunteers who were studied to derive normative data for our laboratory and who were age matched to our patient cohort. The pharyngoesophageal sagittal diameter was measured from the fluoroscopic images at the maximum distension of the narrowest segment of the PEJ, with a correction factor determined from the radio-opaque intraluminal pressure sensors with known diameter.\textsuperscript{29}

\textbf{Endoscopic Dilatation}

A consecutive series of dysphagic laryngectomees underwent an endoscopic examination and dilatation of the PEJ as part of study preliminary to a randomized controlled trial of dilatation, regardless of whether a stricture was apparent radiologically. Subsequent participants were randomized; hence, their data cannot be presented. Dilatation was performed under sedation administered by anesthesiologists using fentanyl, midazolam, and propofol. A diagnostic gastroscope with an outer diameter of 9.2 mm was used (GIF-H190; Olympus Corp, Japan). Dilatation was performed with Savary-Gilliard dilators (Wilson-Cook Medical, Winston-Salem, North Carolina). Selection of the initial dilator size was determined at the time of endoscopy. Our practice is to pass dilators sequentially in increments of 1-mm diameter with periodic inspection following some or all dilator passages until one of the...
following end points is reached: (1) mucosal tear is identified upon reinspection; (2) a maximal dilator diameter of 16 mm is passed; or (3) a total of 3 dilators have passed, including and following the first to meet resistance to passage of the dilator.

HRM with concurrent video fluoroscopy was repeated 3 months after the first dilation, to account for subsequent dilatations that may be required to achieve a satisfactory end point. Patients completed the SSQ predilatation and 2 weeks after every dilatation.

Data Analysis and Statistics

Manometric variables were averaged across bolus volumes for each patient. One-way analysis of variance (ANOVA) with Sidak’s multiple comparison test was used to assess the differences in hPP and hIBP among the controls and patient groups. To determine the bolus volume effect on hPP, hIBP, and pharyngoesophageal sagittal diameter, repeated-measures 1-way ANOVA with Greenhouse and Geisser correction for nonsphericity was utilized. Statistical inferences on the effect of dilatation on SSQ scores and manometric variables were made through Student’s paired t-test.

Linear regression analysis was used to assess the predictive value of hIBP (ΔhIBP) and PEJ sagittal diameter (ΔPEJ sagittal diameter) on symptomatic improvement after dilatation (ΔSSQ score postdilatation). A multivariate analysis was also performed with predilatation hIBP as a predictor of the postdilatation symptoms assessed via SSQ score. SSQ scores at baseline were included in the model as a covariate. All data are presented as mean ± SE.

Results

We recruited 31 patients (74% men; average age, 68 ± 2; range, 49-90 years) who had undergone total laryngectomy 1 to 12 years prior (average, 4 ± 1 years postsurgery). One patient was not included in the study, as he had a completely absent swallow response (SSQ, 1211). Twenty-two (73%) patients had adjuvant postoperative radiotherapy; 4 (13%), preoperative chemoradiotherapy; 2 (7%), preoperative radiotherapy; and 2 (7%), surgery alone.

As predicted from the recruitment sources, the study cohort (n = 30) reported a wide range of dysphagia severity (SSQ) from nil to severe (Figure 2). Twenty-six (87%) patients reported SSQ scores higher than the upper limit of normal (SSQ >234).27 Of 30, 17 (57%) had severe dysphagia (SSQ >500), and 13 (43%) had minor or nil dysphagia (SSQ ≤500).

The effect of swallowed bolus volume on the biomechanical measurements (hIBP, hPP, PEJ sagittal diameter) was assessable in only the 16 patients who were able to tolerate all 3 bolus volumes. Swallowed bolus volume did not affect hPP. The hIBP demonstrated a significant bolus volume dependence, increasing with larger bolus volumes (2 mL: 12 ± 5 mm Hg; 5 mL: 19 ± 6 mm Hg; 10 mL: 27 ± 6 mm Hg; P < .0001, 1-way ANOVA for repeated measures; Figure 3A). Maximum extension of the narrowest PEJ sagittal diameter demonstrated a significant bolus volume
dependency (2 mL: $7 \pm 0.3$ mm; 5 mL: $8 \pm 0.6$ mm; 10 mL: $9 \pm 0.5$ mm; $P < .0001$; Figure 3B) but plateaued at a mean PEJ diameter of 9 mm.

For comparison with control data and for potential correlations with dysphagia severity, we analyzed hIBP and hPP data derived from 5-mL barium swallows for 2 reasons: (1) 14 (47%) patients with severe dysphagia were unable to swallow a 10-mL bolus, and omitting these patients could introduce bias; (2) in the context of significant postswallow pharyngeal residue, 2-mL bolus will be affected by residue to a greater extent than the 5-mL bolus and therefore be less comparable to control data. When compared with that of controls (170 ± 15 mm Hg), hPP in laryngectomees was significantly lower (110 ± 14 mm Hg; $P = .0162$). However, within the patient group, there was no correlation between dysphagia severity and hPP in that hPP was comparable between those with severe (96 ± 15 mm Hg) and mild or nil dysphagia (129 ± 25 mm Hg; not significant; Figure 4). When compared with that of controls (6 ± 5 mm Hg), hIBP was significantly higher in patients (29 ± 5 mm Hg, $P = .0156$; Figure 4B). Within the patient group, patients with severe dysphagia had a significantly higher hIBP than those with mild or nil dysphagia (41 ± 10 vs 13 ± 3 mm Hg, $P = .02$; Figure 4B). The basal PEJ tone of total laryngectomy patients was absent in majority, and for a group, the average basal tone was much lower than the published normal ranges (9 ± 2 vs 82 ± 6 mm Hg, $P < .0001$).

Figure 5 illustrates examples of HRM recordings and videofluoroscopy from 2 cases at opposite ends of the spectrum: (1) severely impaired propulsion without restriction at the PEJ (Figure 5A, 5B) and (2) severe restriction at the PEJ with preserved pharyngeal propulsion (Figure 5C, 5D). This illustrates the typical pathologic manometric patterns and their radiographic correlates. Figure 5A shows no appreciable propagating pharyngeal pressure wave and undetectable basal upper esophageal sphincter pressure. The pale blue section represents weak pharyngeal “pressurization” (synchronous pressure rise along entire pharynx) due, in this case, to some preservation of posterior tongue base motion. Figure 5B is the corresponding fluoroscopic image, showing an adynamic open pharynx (ie, absent progressive pharyngeal constrictor muscle contraction). The “pressurization” seen in Figure 5A is seen throughout the length of the pharynx in the context of no lumen-occluding pharyngeal constriction. Figure 5C demonstrates a preserved progressive pharyngeal contractile pressure wave, ahead of which is a markedly increased hIBP. Note the abrupt drop-off at the level of the PEJ (dashed horizontal line; Figure 5D).

Five patients with dysphagia underwent endoscopic dilatations; in all patients, the end point was reached after a single dilatation session. When compared with baseline, the
average hIBP decreased from 23.0 ± 3 to 17.5 ± 3 mm Hg (P = .0093) following a single endoscopic dilatation session (Figure 6A). This decrement was mirrored by a reduction in SSQ scores from 663 ± 61 predilatation to 378 ± 56 postdilatation (P = .0142; Figure 6B). Dilatation did not significantly affect the hPP (predilatation: 114 ± 30; postdilatation: 88 ± 22 mm Hg).

Following the dilatation, both the decrement in hIBP (ΔhIBP, R² = 0.97, P = .002) and the increment in PEJ sagittal diameter (ΔPEJ sagittal diameter, R² = 0.87, P = .02) correlated significantly with the symptomatic improvement (ie, ΔSSQ; Figure 7A, 7B). The change of hIBP in response to dilatation was significantly correlated with the increment of the sagittal diameter (R² = 0.92, P = .0095; Figure 7C). Predilatation hIBP proved to be a strong predictor of treatment outcome based on the baseline SSQ as a covariate. The equation was computed as follows: post-SSQ score = −27(pre-hIBP) − 0.8(pre-SSQ) − 1499, F(2, 2) = 110.42, P = .009, adjusted R² = 0.98.

Discussion
Total laryngectomy commonly causes pharyngeal dysphagia, which can have a high negative impact on quality of life in these patients.1,2,29 While it has been relatively overlooked and underreported by patients,35,36 recent studies show that pharyngeal dysphagia affects up to 72% of laryngectomees.6 In the present study, in which 87% of laryngectomees had dysphagia, we demonstrated that abnormalities of pharyngeal propulsion as well as PEJ outflow obstruction are important factors contributing to swallow dysfunction. Outflow resistance (hIBP), however, is a strong correlate of dysphagia severity (SSQ) and subsequent response to endoscopic dilatation in this population, while reduced pharyngeal peak contractile pressure is not. SSQ score and hIBP both fell significantly following endoscopic dilatation, yielding a strong correlation between ΔSSQ and ΔhIBP. Importantly, from the clinical standpoint, baseline hIBP was highly predictive of postdilatation SSQ score when baseline SSQ score was a covariate. The postdilatation increment in sagittal PEJ diameter correlated with the decrement in hIBP. These findings are highly relevant clinically because outflow obstruction is the only potentially correctable abnormality, and
dilatation is a simple, safe, and effective therapeutic option in many of these patients.

The findings in the present study, albeit in a very different population, are analogous to earlier studies demonstrating the clinical utility of hIBP in demonstrating pathologic PEJ resistance in patients with dysphagia due to Zenker’s diverticulum. While, unlike laryngectomies, that population generally has preserved pharyngeal propulsion (ie, normal hPP), patients with Zenker’s diverticula also demonstrate a commensurate fall in hIBP with parallel symptomatic improvement following cricopharyngeal myotomy. Although a primary objective of the present study was to show that PEJ resistance is crucial to our understanding of dysphagia in laryngectomies, the data make a strong case for measuring hIBP in these patients as both a diagnostic and prognostic indicator. It might be argued that hIBP is an unnecessary measurement if PEJ strictures are readily detectable radiologically. However, we recently showed, in patients with pharyngeal weakness secondary to head and neck radiotherapy, that radiology is extremely insensitive in detecting PEJ strictures (unpublished data). Hence, HRM can be an important adjunct to contrast radiography particularly when pharyngeal propulsion is markedly impaired.

There are a number of resection-related causes of PEJ outflow obstruction. Simply removing the cricoid cartilage and reconstituting what was previously an oval configuration into a circular configuration will reduce luminal caliber at the cricopharynx. Loss of extrinsic hyolaryngeal tractional forces on the upper esophageal sphincter can impair the extent of opening of the PEJ. Additionally, adjuvant radiotherapy can stimulate fibrogenesis, thereby causing fibrosing PEJ strictures. Damage to pharyngeal nerves may adversely affect the vigor of pharyngeal contraction during the swallow. Such damage may be a consequence of surgical damage (specifically to muscles important to the generation of pharyngeal contraction pressure) or may be further compounded by radiotherapy-related nerve and muscle damage in those receiving radiotherapy.

In conclusion, the pathophysiology of pharyngeal dysphagia in laryngectomies is multifactorial and includes both impaired pharyngeal propulsion (reduced hPP) and increased pharyngeal outflow resistance (increased hIBP). Detecting and quantifying outflow resistance is vital because (1) it is the major contributing factor of dysphagia in many, (2) it is amenable to simple and effective treatment (endoscopic dilatation), and (3) baseline measurement of the resistance is predictive of treatment outcome and can provide evidence of obstruction.
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; Michal 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; Julia Maclean, videofluoroscopy analysis, quality assurance, manuscript review and final approval, agreement to be accountable for all aspects of the work; Paul Bertrand, 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; Taher Omari, 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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