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Biomechanics of Pharyngeal Deglutitive Function Following Total Laryngectomy

Teng Zhang[13], Michal Szczesniak[13], Julia Maclean[2], Bertrand P[4], Peter I Wu[13], Taher Omari[5], Ian J Cook[13].

Dept. Gastroenterology & Hepatology[1] & Dept. Speech Pathology[2], St George Hospital, Sydney; School of Medicine University of New South Wales[3], Sydney; School of Medical Science University of RMIT[4], Melbourne; School of Medical Science University of Adelaide[5].

Keywords:

Address for Correspondence:

Prof Ian J Cook. Director of GI Motility Service

Teng Zhang. Research officer

Dept. Gastroenterology & Hepatology, Level 1, Burt Wing,

St George Hospital, Gray St, Kogarah 2217

Australia

Tel: +61 2 9113 2817, Fax: +61 2 9113 3993

Email: i.cook@unsw.edu.au; teng.zhang@unsw.edu.au;

ABSTRACT

Objective: Post-laryngectomy surgery, pharyngeal weakness and pharyngoesophageal junction (PEJ) restriction are the underlying candidate mechanisms of dysphagia. We aimed to determine, in laryngectomees whether: 1) hypopharyngeal propulsion is reduced and/or PEJ resistance is increased; 2) endoscopic dilatation improves dysphagia; and 3) if so, whether symptomatic improvement correlate with reduction in resistance to flow across the PEJ.

Methods: Swallow biomechanics were assessed in 30 total laryngectomees. Average peak contractile pressure (hPP) and hypopharyngeal intrabolus pressure (hIBP) were measured from combined high resolution manometry and video-fluoroscopic recordings of barium swallows (2, 5&10ml). Patients were stratified into severe dysphagia (Sydney Swallow Questionnaire (SSQ)>500) and mild/nil dysphagia (SSQ≤500). In 5 patients, all measurements were repeated after endoscopic dilatation.

Results: Dysphagia was reported by 87%, and 57% had severe and 43% had minor/nil dysphagia. Laryngectomees had lower hPP than controls (110 ± 14mmHg vs 170 ± 15mmHg; $p<0.05$), while hIBP was higher (29 ± 5mmHg vs 6 ± 5mmHg; $p<0.05$). There were no differences in hPP between patient groups. However, hIBP was higher in severe than in mild/nil dysphagia (41 ± 10mmHg vs 13 ± 3mmHg; $p<0.05$). Pre-dilation hIBP ($R^2=0.97$) and its decrement following dilatation ($R^2=0.98$) were good predictors of symptomatic improvement.

Conclusion: Increased PEJ resistance is the predominant determinant of dysphagia as it correlates better with dysphagia severity than peak pharyngal contractile pressure. While both baseline PEJ resistance and its decrement following dilatation are strong predictors of outcome following dilatation, the peak pharyngeal pressure is not. PEJ resistance is vital to detect as it is the only potentially reversible component of dysphagia in this context.

INTRODUCTION

Respiratory, phonatory and deglutitive functions of the laryngectomees are dramatically altered {Blom, 1996 #14254} leading to significant morbidity {Starmer, 2008 #13842}. Total laryngectomy involves surgical excision of the larynx and epiglottis, as well as strap muscles, thyroid and cricoid cartilage, hyoid bone, and up to two proximal tracheal rings {Savary, 1975 #14065} {Agrawal, 2008 #13841}{Lefebvre, 2012 #13840} {Agrawal, 2008 #13841}. The precise nature and extent of the surgery and post-resection pharyngeal closure vary markedly depending upon tumour extent and surgeon preference {Maclean, 2009 #13961}. Wherever possible, adequate pharyngeal mucosa is preserved to ensure satisfactory post-operative phonation and deglutition functions {Brok, 1998 #14066}.

Dysphagia following laryngectomy is common with the reported prevalence varying widely from 17 - 72% {Maclean, 2009 #13961} {Ward, 2002 #12477} {Ward, 2002 #12477} {Vu, 2008 #13845} {Ward, 2002 #12477}. The cause of dysphagia is multifactorial. Impaired pharyngeal propulsion can result from surgical damage to the pharyngeal muscles compounded by adjuvant radiation-related neuromuscular dysfunction {Laurell, 2003 #13474} {Lee, 2006 #13489}. Contributory causes of increased outflow resistance across the PEJ include reduced calibre of the PEJ resulting from removal of the cricoid cartilage, and loss of extrinsic hyolaryngeal tractional forces on the UES {Welch, 1979 #13967} {Welch, 1979 #13965} {Roed-Petersen, 1979 #13968} {McConnel, 1986 #13969}. Additionally, adjuvant radiotherapy, administered in up to 84% of late stage laryngeal cancers patients, can create fibrosing PEJ strictures {Mendenhall, 1990 #14387} {Mayberry, 2001 #14266} {Castell, 1976 #1308}.

The biomechanics of deglutition following laryngectomy has received little attention. We know, from early manometric studies in laryngectomees, that pharyngeal neuromyopathic dysfuntion results in reduction of the pharyngeal contractile pressure {Welch, 1979 #13967} {Welch, 1979 #13965}{Collo, 1977 #13964} {Walther, 1993 #13972} {Lazarus, 2002 #13998} {McConnel, 1988 #13971} and that bolus transition time during pharyngeal deglutitive phase is increased {McConnel, 1987 #13970} {McConnel, 1988 #13971}. However, the clinical relevance of these manometric and temporal findings remains unclear as none related these parameters specifically to 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 overall 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 whether: 1) hypopharyngeal prolusion is reduced or PEJ resistance is increased and the relative importance of these two biomechanical parameters; 2) symptomatic improvement following dilatation correlates with reduction in resistance across the PEJ and can be predicted by pre-dilatation biomechanical measures.

METHODS

<u>Patients</u>

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 tumour recurrence or any neurological disorder potentially associated with dysphagia (eg. prior cerebrovascular accident, Parkinson's disease, myopathy etc.), or known oesophageal pathology causing dysphagia (eg. oesophageal stricture, malignancy).

<u>Dysphagia severity</u>

Dysphagia severity was assessed using the Sydney Swallow Questionnaire (SSQ) {Wallace, 2000 #7618} a validated self-reporting swallowing assessment tool for oral-pharyngeal dysphagia which has also been validated in a head and neck cancer population {Dwivedi, 2010 #14136}. The SSQ scores range from 0 to 1700, with an upper limit of normal being 234 {Szczesniak, 2014 #14143}. Patients were stratified into two 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 vast majority of patients with self-reported moderate to severe dysphagia have SSQ scores over 500.

<u>Biomechanical measurements</u>

Pharyngeal propulsion and PEJ resistance were assessed using high resolution manometry (HRM) combined with concurrent video fluoroscopy as described previously {Szczesniak, 2015 #14295} {Maclean, 2011 #13824}. Briefly, with participants seated upright, the manometry catheter (Unisensor USA Inc, Portmouth, NH, USA) with a diameter of 3.6mm incorporating 25 solid-state pressure sensors at 1 cm spacing was positioned transnasally to span the pharynx and the PEJ after topical nasal anesthesia (lignocaine 10%). Videofluoroscopic cine-loops were acquired (MultiDiagnost Eleva; Philips, Best, The Netherlands) and recorded concurrently with HRM using an MMS Solar GI system (Software Version 8.21o; MMS, Enschede, The Netherlands). Participants swallowed triplicate boluses of 2, 5, and 10 mL of EZ-HD barium (Bracco UK Limited, Woodburn Green, High Wycombe, UK).

The manometric marker of PEJ resistance was the hypopharyngeal intrabolus pressure (hIBP), defined as the pressure within the advancing bolus measured 1cm above the upper border of the PEJ at the midpoint of bolus flow through the PEJ (Fig 1) {Cook, 1992 #5850}. The manometric measure of pharyngeal propulsion was peak pharyngeal (contractile) pressure (hPP) {Cook, 1992 #5850} {Cook, 1992 #5853} {Omari, 2011 #13774} defined as the average of peak pressures recorded across a 3cm segment above the upper margin of the PEJ at its apogee of upward excursion during the swallow {Omari, 2014 #14147} (Fig 1). Control manometric measures were obtained from 11 healthy aged volunteers studied in order to derive normative data for our laboratory and who were age-matched to our patient cohort.

The pharyngoesophageal (PE) sagittal diameter was measured from the fluoroscopic images at the maximum distension of the narrowest segment of the pharyngoesophageal junction (PEJ), using a correction factor determined from the radio-opaque intraluminal pressure sensors with known diameter {Maclean, 2011 #13824}.

Endoscopic Dilatation

A consecutive subgroup of dysphagia patients underwent an endoscopic examination and dilatation of the stricture as part of study preliminary to a randomized controlled trial of dilatation. 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 9.2mm was used (Olympus GIF-H190, Olympus Corp, Japan). Dilatation was performed using Savary-Gilliard dilators (Wilson-Cook Medical, Winston-Salem, NC, USA). Selection of the initial dilator size was determined at the time of endoscopy. Our practice is to pass dilators sequentially in increments of 1mm diameter with periodic inspection following some or all dilator passages until one of the following endpoints is reached: 1) mucosal tear identified upon re-inspection; or 2) a maximal dilator diameter of 16mm is passed; 3) a total of 3 dilators passed including and following the first to meet resistance to passage of the dilator.

Patients completed the SSQ pre-dilatation and two weeks post treatment. HRM with concurrent video fluoroscopy were repeated 3 months post-dilation.

Data analysis and Statistics

Manometric variables were averaged across bolus volumes for each patient. One-Way ANOVA with Sidak's multiple comparison test was used to assess the differences in hPP and the hIBP among the controls and patient groups. To determine the bolus-volume effect on hPP, hIBP and PE sagittal diameter, repeated measures one-way ANOVA with Greenhouse and Geisser correction for non-sphericity. Statistical inferences on the effect of dilatation on SSQ scores and manometric variables were made using 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 post dilatation). A multivariate analysis was also performed using pre-dilatation hIBP as a predictor of the post-dilatation symptoms assessed using 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% male, average age 68 ± 2; range 49 – 90yrs) who had undergone total laryngectomy 1–12yrs prior (average 4±1yrs post-surgery). One patient was not included in the study as he had a completely absent swallow response (SSQ 1211). Twenty-two (73%) patients had had adjuvant postoperative radiotherapy, 4 (13%) had preoperative chemo radiotherapy, 2 (7%) had preoperative radiotherapy while 2 (7%) had 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 (Fig2). Twenty six (87%) patients reported SSQ scores

higher than the upper limit of normal (SSQ > 234) {Szczesniak, 2014 #14143}. Seventeen of 30 (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, PE sagittal diameter) was only assessable in the 16 patients who were able to tolerate all three bolus volumes. Swallowed bolus volume did not impact hPP. The hIBP demonstrated a significant bolus volume-dependence, increasing with a larger bolus volumes (2ml: 12±5mmHg, 5ml: 19±6mmHg, 10ml: 27±6 mmHg, p<0.0001, one way ANOVA for repeated measures) (Fig 3 A). Maximum PEJ sagittal diameter demonstrated a significant bolus volume-dependency (2ml: 7±0.3mm, 5ml: 8±0.6mm, 10ml: 9±0.5mm; p<0.0001), but plateaued at a mean PEJ diameter of 9mm.

For comparison with control data and for potential correlations with dysphagia severity, we only analysed hIBP and hPP data derived from 5mL barium swallows because: 1) 14 (47%) patients with severe dysphagia were unable to swallow a 10mL bolus, omitting these patients could introduce bias; 2) in the context of significant post-swallow pharyngeal residue 2m bolus will be affected by residue to a greater extent than the 5ml bolus and therefore less comparable to control data. When compared with controls (170±15mmHg), hPP in laryngectomees was significantly lower (110±14mmHg; p<0.05). However, within the patient group there was no correlation between dysphagia severity and hPP, in that hPP was comparable between those with severe (96 ±15mmHg) and mild or nil dysphagia (129±25mmHg; p=NS) (Fig 4). When compared with controls (6±5mmHg) hIBP was significantly higher in patients (29±5 mmHg, p<0.05) (Fig 4B). Within the patient group, patients with severe dysphagia had a significantly higher hIBP than those with mild or nil dysphagia (41±10mmHg vs 13±3mmHg, p<0.05) (Fig 4B).

Figure 5 illustrates examples of HRM recordings and videofluroscopy from two cases at opposite ends of the spectrum: 1) severely impaired propulsion without restriction at the PEJ and 2) severe restriction at the PEJ with preserved pharyngeal propulsion. This illustrates the typical pathological manometric patterns and their radiographic correlates.

Five patients with dysphagia underwent endoscopic dilatation. When compared with baseline the average hIBP decreased from 23.0±2.79mmHg to 17.5±3.05mmHg (p<0.05) following a single endoscopic dilatation session (Fig 6A). This decrement was mirrored by a reduction in SSQ scores from 663±55 pre-dilatation to 378±50 post-dilation (p<0.05) (Fig 6B). Dilatation did not impact significantly the hPP (pre-dilatation 23±SE2.79mmHg vs post-dilatation 17.5±SE3.06mmHg).

Following the dilatation, both the decrement in hIBP (ΔhIBP, R^2=0.97) and the increment in PEJ sagittal diameter (ΔPEJ sagittal diameter, R^2=0.87) correlated significantly with the symptomatic improvement (ie ΔSSQ) (p<0.05) (Fig 7). Pre-dilatation hIBP proved to be a strong predictor of treatment outcome using the baseline SSQ as a covariate. The equation was computed to be PostSSQ score =-27hIBPpre – 0.8PreSSQ – 1499, $F_{(2,2)}$ = 110.42, p < 0.01, adj R^2 = 0.98.

DISCUSSION

Total laryngectomy commonly causes pharyngeal dysphagia which can have a very high negative impact on quality of life in these patients {Maclean, 2011 #13824}{Blom, 1996 #14254}{Starmer, 2008 #13842}. While it has been relatively overlooked and under-reported by patients {Samlan, 2002 #13843} {Manikantan, 2009 #13750} recent studies show it affects up to 72% of laryngecomees {Maclean, 2008 #12258}. In the present study, in which 87% of laryngectomees had dysphagia, we have demonstrated that abnormalities of both pharyngeal propulsion as well as PEJ outflow obstruction are important determinants of swallow dysfunction. Outflow resistance (hIBP), however, is a strong correlate of both 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 post-dilatation SSQ score when using baseline SSQ score as a covariate. The post-dilatation 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 pathological PEJ resistance in patients with dysphagia due to Zenker's diverticulum {Cook, 1992 #5850}. While unlike laryngectomees, 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 {Shaw, 1996 #6853}. While a primary objective of the present study was to show that PEJ resistance is crucial to our understanding of dysphagia in laryngectomees these data also 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 have recently shown in patients with pharyngeal weakness secondary to head and neck radiotherapy that radiology is extremely insensitive in detecting PEJ strictures {Szczesniak, 2015 #14397}. Hence, high resolution manometry 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 calibre at the cricopharyngeus {Welch, 1979 #13967} {Welch, 1979 #13965} {Roed-Petersen, 1979 #13968}. Loss of extrinsic hyolaryngeal tractional forces on the upper esophageal sphincter can impair the extent of opening of the PEJ {Duranceau, 1976 #13975} {McConnel, 1986 #13969} {McConnel, 1988 #13971}. Additionally, adjuvant radiotherapy can stimulate fibrogenesis {Paulsen, 1999 #14184}thereby causing fibrosing PEJ strictures {Mendenhall, 1990 #14387} {Mayberry, 2001 #14266} {Castell, 1976 #1308} {Lee, 2006 #13489}. Damage to pharyngeal nerves may be adversely impact the vigour of pharyngeal contraction during the swallow {Kitagawa, 2002 #11055}. Such damage may be consequence of surgical damage (specifically to muscles important to the generation of pharyngeal contraction pressure) or further compounded by radiotherapy-related nerve and muscle damage in those receiving radiotherapy {Laurell, 2003 #13474} {Lee, 2006 #13489} {Piotet, 2008 #13475} {Nguyen, 2008 #13505} {Mayberry, 2001 #14266}.

The findings of the present study suggest that surgeons might explore alternatives or modifications to current approaches to resection and closure. For example, if feasible, preservation of the hyoid bone and its connections of the hyolaryngeal suspensory muscles (mandible anteriorly and skull base posteriorly) and those connections with the PEJ might be considered. The impact of closure technique on the calibre of the hypopharynx and the integrity of contractile mechanics the pharyngeal constrictors needs to be considered also. For example, Maclean et al found that, when compared with mucosal closure alone, combined mucosal and muscle closure results in significantly higher mid pharyngeal pressures during the swallow and reduced post swallow residual {Maclean, 2011 #13974}.

Although not widely adopted, dilatation in the treatment of strictures in laryngectomees using Savary dilators has reported response rates as high as 75-84% with no perforations, bleeding or deaths in those two studies {Dhir, 1996 #14396} {Ahlawat, 2008 #14395}. Alternative dilatation techniques report comparable outcomes {Kozarek, 1984 #14394} {Harris, 2010 #13848} {Cho, 2010 #13849}. Strictures forming in patients who have undergone adjuvant chemotherapy may be more recalcitrant, necessitating more frequent dilatations {Nguyen, 2004 #12256}. While in the present study we have reported symptom (and biomechanical) outcome following a single endoscopic dilatation session in only 5 patients, in our experience, these patients often require repetitive stepwise dilatations to achieve a satisfactory and durable outcome. A randomised efficacy study is in progress, but an earlier open label study found that these patients required an average of 3 dilatation sessions to achieve a response with a range of 1 -12 sessions {Paramsothy, 2012 #13830}.

In conclusion, the pathophysiology of pharyngeal dysphagia in laryngectomees is multifactorial and includes both impaired pharyngeal propulsion and increased pharyngeal outflow resistance. Detecting and quantifying outflow resistance is vital because: it is the major contributing factor in many; it is amenable to simple and effective treatment (endoscopic dilatation) and baseline measurement of this obstruction is predictive of treatment outcome and can provide evidence of obstruction when radiology may not.

REFERENCES:

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FIGURE LEGENDS

Fig 1: Example of high resolution manometry isocontour plot with concurrent video fluoroscopy. In this normal case, A) when swallow is initiated the PEJ is relaxed before arrival of the bolus head; B) during bolus passage through the PEJ, minimal intrabolus pressure (hIBP) can be seen (E) in this case; C) the tail of the bolus is leaving the PEJ ahead of the propagating pharyngeal striping wave, at this point the PEJ remains at the apogee of its upward axial excursion D) the bolus has been cleared from the pharynx and the PEJ returned to its resting position. Key measurements are (E)= hIBP and (F) = hPP.

Fig 2: The range of SSQ scores in 31 laryngectomees. The mean SSQ score for the cohort is 718±SE79. Only 13% of patients reported scores in the normal range. The dashed lines represent the threshold for moderate-severe dysphagia (>500). NUL = normal upper limit

Fig 3: Bolus volume effect on pharyngeal biomechanical measures. hIBP (A) and PEJ sagittal diameter (B) increases significantly with increased swallowed bolus volume (*p<0.0001, one way ANOVA for repeated measures). PEJ sagittal diameter shows a plateau effect beyond 5ml volume. hPP was not affected by bolus volume (NS).

Fig 4: The relationship of dysphagia severity and biomechanical measures. A: Patients following laryngectomy have lower hypopharyngeal peak pressure (hPP) than controls but there was no correlation between dysphagia severity and hPP. B: Laryngectomees have higher PEJ resistance (ie higher hIBP) than controls. Note also, that hIBP in patients with severe dysphagia was significantly higher than those the mild or nil dysphagia. *p<0.05, NS=No Significance.

Fig 5: Two distinctly different examples of biomechanical perturbations in laryngectomees. A&B: HRM from a case with weak pharyngeal propulsion and no PEJ obstruction. A: This shows no appreciable propagating pharyngeal pressure wave and undetectable basal UES 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. B: Corresponding fluoroscopic image showing an adynamic open pharynx (ie absent progressive pharyngeal constrictor muscle contraction). The "pressurization" seen in A is seen throughout the length of the pharynx in the context of no lumen-occluding pharyngeal contraction. C & D: HRM from case with preserved pharyngeal propulsion and significant PEJ obstruction. C: This 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 stricture (dashed horizontal line) (D).

Fig 6: Impact of dilatation (n = 5) on symptoms and biomechanical parameters. Symptom scores improved. The hIBP fell significantly while hPP was unaffected by dilatation. *p<0.05; **p<0.01; NS=Not significant.

Fig 7: Correlations between the objective measures and the symptomatic improvement in response to dilatation. Improved SSQ scores correlate with decrement in IBP (R^2=0.97, p<0.01) and increment in PEJ sagittal diameter (R^2=0.87, p<0.05).
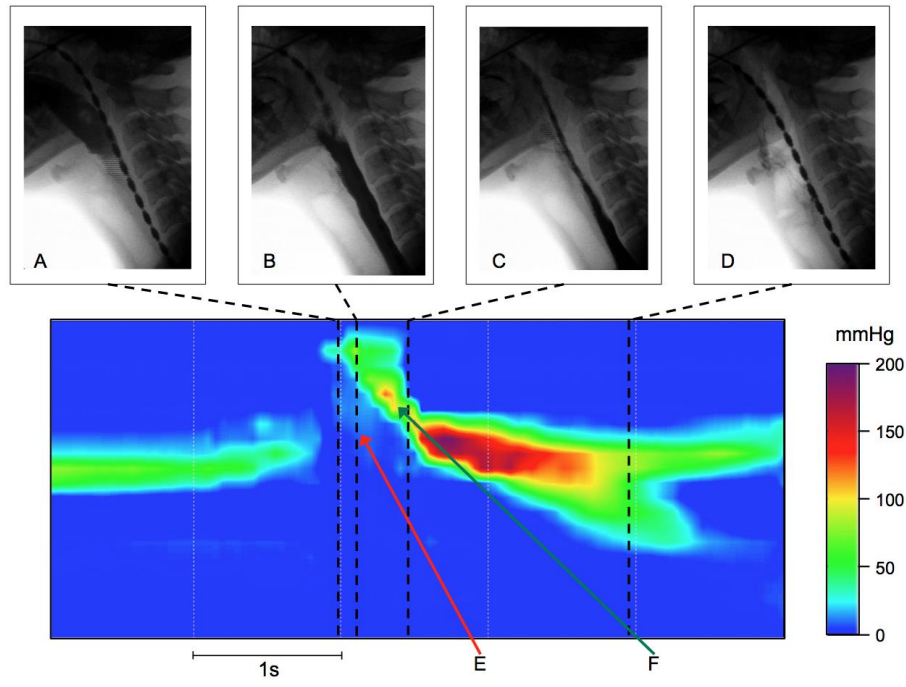
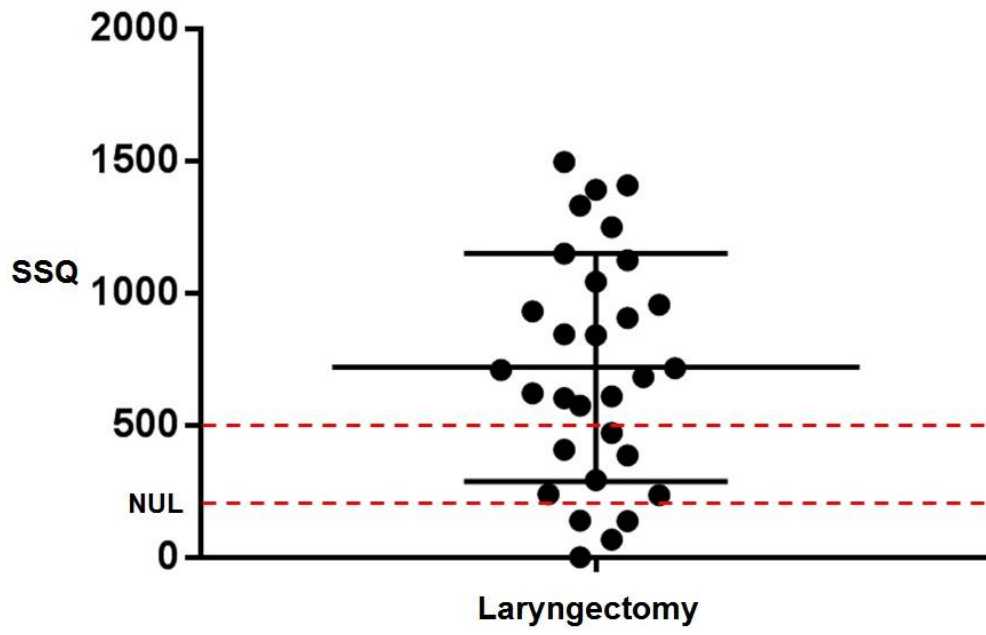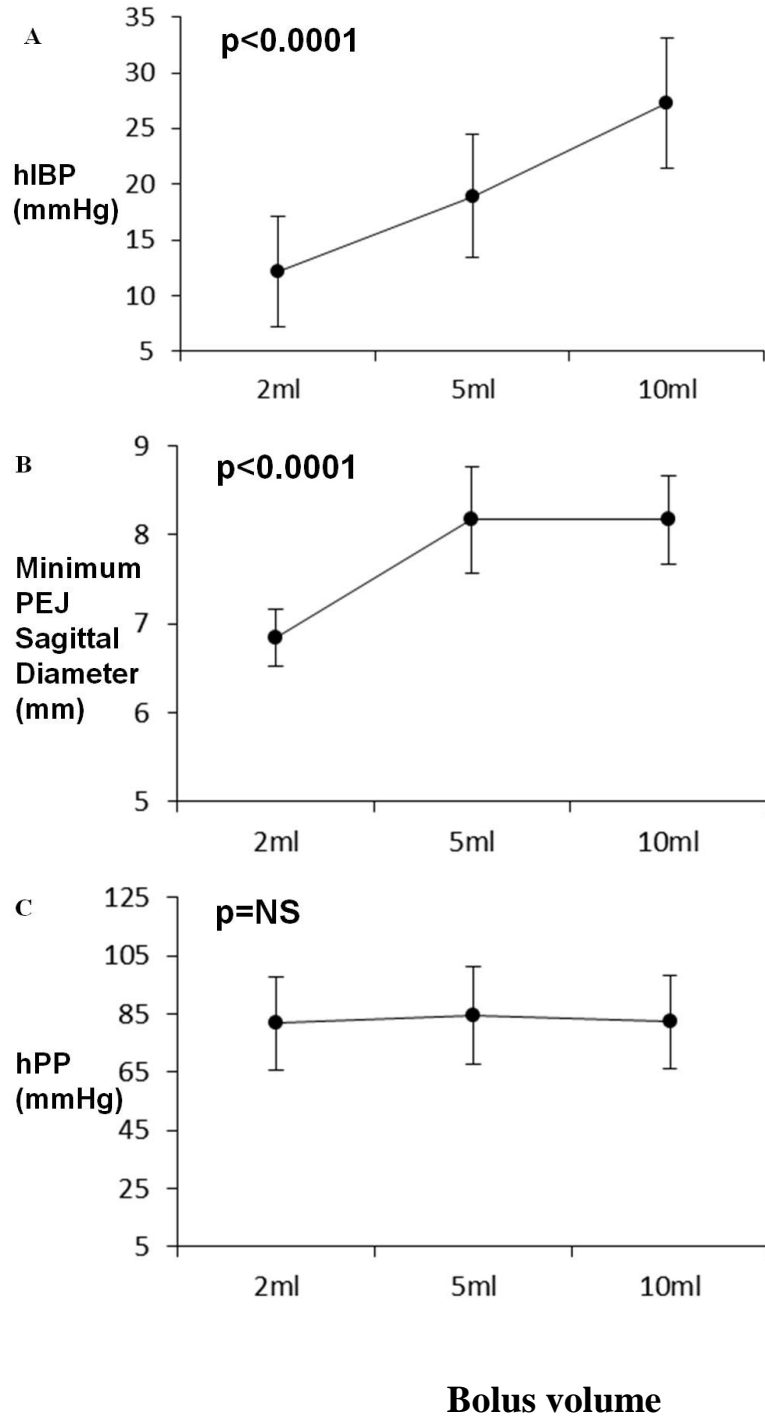Fig 1

Fig 2

Fig 3

Bolus volume

Fig 4

Fig 5

Fig 6

Fig 7

A

y = 56.90x - 27
R² = 0.97
p<0.01

B

y = 64.73x + 131
R² = 0.87
p<0.05