A NEW EVALUATION OF THE UPPER ESOPHAGEAL SPHINCTER USING THE FUNCTIONAL LUMEN IMAGING PROBE- A PRELIMINARY REPORT

Running Title: FLIP Evaluation of Upper Esophageal Sphincter

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Abstract

Background: Objective and reliable evaluation of UES opening during swallowing based on videofluoroscopy and pharyngeal manometry challenges dysphagia clinicians. The Functional Lumen Imaging Probe (FLIP) is a portable tool based on impedance planimetry originally designed to measure esophogastric junction compliance. It is hypothesised that FLIP can evaluate UES distensibility and can provide UES diameter and pressure measurements at rest, during swallowing and during voluntary manoeuvres.

Methods: Eleven healthy adult subjects consented to FLIP evaluation. The probe was inserted trans-orally and the balloon positioned across the UES. Two twenty millilitre ramp distensions were completed. Changes in UES diameter and intra-balloon pressure were measured during dry and 5ml liquid swallows and during voluntary swallow postures and manoeuvres employed in clinical practice.

Results: The protocol was completed by ten of eleven healthy subjects. Mean intra-balloon pressure increased throughout 5ml (5.8mmHg; -4.5-18.6mmHg), 10ml (8.7mmHg; 2.3-28.5mmHg), 15ml (17.3mmHg; 9.5-34.8mmHg) and 20ml (25.2mmHg; 16.8-40.1mmHg) balloon volumes. Mean resting UES diameter (4.9mm) increased during dry swallows (9.2mm) and 5ml liquid swallows (7.7mm). Mean UES diameter increased during 5ml liquid swallows with head turn to right (8.1mm) and left (8.3mm), chin tuck (8.4mm), effortful swallow (8.5mm), Mendelsohn manoeuvre (8.1mm) and supraglottic swallow (7.8mm).

Conclusions: FLIP was safely inserted and distended in the UES and provided useful quantitative data regarding UES distensibility and UES diameter changes during swallowing manoeuvres. Further research is being conducted to explore the role of FLIP in UES evaluation.

Key words: upper esophageal sphincter, dysphagia, evaluation, Functional Lumen Imaging Probe

Background

Patterns and mechanisms of upper esophageal sphincter (UES) opening are still not fully understood. During swallowing, cricopharyngeal muscle relaxation is closely followed by anterior and superior hyo-laryngeal excursion which stretches open the UES. Pressure from the on-coming bolus further distends the UES to approximately 8mm, and then the UES closes all within 0.5 seconds (Figure 1)(1, 2). Inter-rater reliability of UES opening measures based on two-dimensional videofluoroscopy images is poor(3). Currently, there is no diagnostic method capable of objectively differentiating between each phase of UES opening. A better understanding of UES function could improve the rehabilitative or surgical treatment of aspiration and inefficient bolus clearance in individuals with dysphagia.

FIGURE 1 HERE

The functional lumen imaging probe (FLIP) is a novel distensibility evaluation technique based on the principles of impedance planimetry (4). FLIP was first used to evaluate esophogastric junction (EGJ) distensibility, and has since evaluated the upper esophagus, the sphincter of Oddi and laparoscopic lumens (4-8). To date, no studies have investigated the role of FLIP in evaluating UES function. Videofluoroscopy studies have demonstrated safe insertion and distension of the FLIP balloon in the UES of patients with dysphagia (Figure 2C) (9). The aims of this exploratory study were to use FLIP to (i) to derive preliminary data on UES distensibility and (ii) to measure UES diameter and intra-balloon pressure at rest, during swallowing and

during voluntary manoeuvres previously described in a pilot group of healthy subjects (10).

Methods

Subjects

Subjects were recruited from a pool of healthy volunteers. Inclusion criteria were (1) no history of oro-pharyngeal or oesophageal dysphagia, (2) no history of gastrointestinal, neurological or respiratory disease (3) no history of head and neck cancer or ear nose and throat conditions. Eleven healthy adults (three male), with a mean age of 34 years (range 20-50; standard deviation (SD) 11.3) met inclusion criteria. Written consent was obtained from subjects. Before each FLIP evaluation, all voluntary swallowing manoeuvres included in the assessment were explained and demonstrated to subjects. Ethical approval was obtained from the Research Ethics Committee, University Hospitals Leuven, Belgium.

FIGURE 2 HERE

EndoFLIP® System

A commercially developed FLIP (EndoFLIP® system, Crospon Ltd., Galway, Ireland) was used (Figure 2A). A polyutherane balloon with a maximum volume of 60 ml was mounted on the distal 14 cm of a probe (EF-325) (length 240cm, diameter 25mm) attached to the EndoFLIP® unit (Figure 2B). This balloon assumes a 10cm long cylindrical shape with maximum diameter of 2.5 cm. The maximum balloon diameter was critical to prevent

airway compromise during balloon distension. Across an 7.5cm segment within the balloon, 17 ring electrodes were spaced 5mm apart to obtain 16 impedance planimetry measurements (Figure 2B). This allowed diameter and pressure changes above (i.e. pharynx) and below (i.e. upper esophagus) the UES to be captured and for UES opening to be observed despite its upward shift during swallowing. Excitation electrodes situated at either end of the 17 ring electrodes emitted a constant low electrical current within the balloon. The probe also contained a solid-state pressure transducer to measure intra-balloon pressure.

Protocol

The EndoFLIP® system was positioned beside the subject who was seated upright on a chair within the clinic room (Neurogastroenterology & Motility Clinic, University Hospital Leuven). The equipment was powered on and both the syringe and a pre-calibrated probe were connected to the EndoFLIP® unit. An automated purge sequence initiated by the EndoFLIP® removed air from the balloon. Topical anaesthesia (Lignocaine spray) was administered to the posterior pharyngeal wall and subjects were instructed to swallow. The tip of the FLIP probe was lubricated and inserted orally by a member of the research team until the balloon at the distal end of FLIP was judged to have passed into the proximal esophagus (30cm marking on FLIP catheter). The subject was transferred to a bed and seated in a 90 degree angle upright position. The FLIP catheter was placed outside of the subjects'

teeth and held by a researcher to minimize displacement during the evaluation.

When the subject was accustomed to the probe, the probe balloon within the esophagus was distended with 10mls saline solution from the syringe using a touch screen function on the EndoFLIP® monitor. The inflated balloon was slowly retracted until the hourglass shape of the UES could be visualised on the EndoFLIP® screen (17-20cm marking on FLIP catheter) (Figure 2D). This confirmed the balloon position in the UES. While holding the catheter in place, the balloon was deflated by pressing the touch screen control on the unit monitor.

After a brief habituation period (1-2 minutes), two 20ml ramp distensions were completed (rate 60ml/minute). Subjects were requested not to swallow during distensions and the EndoFLIP® screen was monitored to ensure the balloon remained in position. The balloon was re-inflated with either 12ml or 15mls conductive solution (balloon volume was reduced to 12mls after two studies to optimise tolerance). Once a baseline measure of minimum UES diameter (mm) and intra-balloon pressure (mmHg) was recorded, subjects were asked to complete the following:

(a) dry swallow

(b) 5ml liquid swallow delivered orally via a syringe

(c) voluntary swallow manoeuvres during 5ml liquid swallows delivered orally via syringe: (i) swallow with head turn to left; (ii) swallow with head turn to

right; (iii) swallow with chin tuck; (iv) effortful swallow; (v) swallow with Mendelsohn manoeuvre and (vi) supraglottic swallow.

A minimum 10 second time period between the performances of each strategy was enforced to easily identify manoeuvres during data analysis. The time (in seconds) displayed on the EndoFLIP® device at the execution of each manoeuvre was recorded. When the protocol was completed, the balloon was deflated and the probe was removed.

Data Analysis

To evaluate UES distensibility, mean cross-sectional area and intra-balloon pressure measures were determined at 5, 10, 15 and 20ml volumes. Using times (in seconds) recorded from the EndoFLIP® unit, measures of (i) minimum UES diameter (mm) and (ii) minimum intra-balloon pressure (mmHg) were attained at baseline, during dry and liquid swallowing and during voluntary manoeuvres. Descriptive statistics were used to analyse results.

Results

TABLE 1 HERE

Ten of eleven subjects completed the study protocol. Subject 2 did not complete the study due to intolerance of the distended balloon in the UES for a prolonged period. Subject 1 did not complete voluntary postures and manoeuvres during 5ml liquid swallows as it was only upon completion of this

initial study that authors ascertained that liquid could be swallowed with the balloon distended in the UES and then extended the protocol for subsequent studies.

FIGURE 3 HERE

During 20ml ramp distensions, the EndoFLIP® balloon assumed an hourglass shape at the level of the UES across all subjects (Figure 3). Mean increases in intra-balloon pressure and cross-sectional area during ramp distensions are detailed in Table 1.

TABLE 2 HERE

FIGURE 4 HERE

Figure 4 demonstrates changes in mean UES diameter (mm) and intra-balloon pressure (mmHg) during dry swallows and 5ml liquid swallows. Prolonged UES opening time in two cases (3, 4) may represent a struggling behaviour in initiating a pharyngeal swallow. Table 2 summarises effects of voluntary manoeuvres on UES diameter and intra-balloon pressure during 5ml liquid swallows. The effects of swallow manoeuvres on EndoFLIP® geometric profile of the UES (subject 1) in an individual participant is detailed in Figure 5.

FIGURE 5 HERE

Discussion

This preliminary study tested the use of FLIP to evaluate UES dynamics in a pilot group of healthy subjects. The FLIP balloon was positioned and distended in the UES without fluoroscopic guidance and studies were completed without incident or adverse event. While all subjects tolerated FLIP placement in the UES region, one of eleven subjects could not tolerate the inflated probe in the UES for prolonged periods to complete the study protocol. Further studies will need to be completed to establish tolerance levels.

During distensibility testing, ramp distensions were conducted to a lower maximum volume (20ml) than EGJ studies to ensure the airway was not impinged. Nevertheless, the hourglass shape of the UES could be observed across subjects (Figure 3) and mean intra-balloon pressure and UES CSA increased across 10, 15 and 20ml volumes (Table 1).

Maximum UES diameters during dry and liquid swallowing as measured by FLIP are similar to videofluoroscopy measures (2)(Figure 1). Albeit with varying balloon volumes (12 or 15mls), FLIP also established mean effects of voluntary manoeuvres on extent of UES opening (Table 2). Effectiveness of strategies could be determined within evaluations due to real-time geometric profile of the UES on the EndoFLIP® screen.

Of note, the minimal detectable diameter of the EndoFLIP probe is 4.8mm (or 18.1mm^2) because of its physical size. Therefore, if the probe measures 4.8mm the actual value may be smaller than that. This is a source of error which may make the deviation of data for these small measurements seem less than it actually is. Additionally, FLIP does not provide real information on the actual luminal shape in the UES region. However, from this and studies of other regions (i.e. EGJ), we know it is representative of function, particularly as it relates to the distension required to open the sphincter and representing that opening as a measure of multiple radial cross sectional areas.

In future studies, confounding effects of factors (e.g. anxiety) on UES measurement should be minimised (e.g. habituation period). Optimal balloon positioning and volume during testing need to be established. Reproducibility of FLIP data and most appropriate data analysis require investigation.

Preliminary findings suggest that FLIP can provide novel and clinically useful quantitative measures regarding UES dynamics. Objective information regarding UES opening is clinically valuable and is lacking due to subjectivity and poor inter-reliability of videofluoroscopic analysis(3). Research is currently underway to further explore the role of FLIP in UES evaluation**.**

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Competing Interests: BM previously worked as a consultant for Crospon Ltd and is currently a minor shareholder in Crospon Ltd.

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Tables

Table 1. Change in UES Cross-Sectional Area and Intra-Balloon Pressure During 20ml Ramp Distension (N=10)

	Pressure (mmHg)				***Cross-sectional area (mm^2)***			
EndoFLIP Balloon Volume (ml)	**mean**	**SD**	**min**	**max**	**mean**	**SD**	**min**	**max**
5	5.8	7.7	-4.5	18.6	20.9	1.9	18.5	23.5
10	8.7	8.7	-3.5	28.5	22.1	2.2	19.1	25.5
15	17.3	7.9	8.8	34.8	23	2.8	19.7	28.4
20	25.2	8	16	40.1	23.5	2.8	20.2	28.4

Table 2. UES Diameter & Intra-Balloon Pressure Changes During Swallowing

Manoeuvre		***N***	***Mean Minimum UES Diameter (mm)***	***Mean Minimum Intra-Balloon pressure (mmHg)***
At Rest		10	4.9mm (4.8-5, SD: 0.1)	30.2mmHg (18.2-62.9, SD: 14.7)
Dry Swallow		10	9.2mm (5.2-11.6, SD: 2)	8.6mmHg (3-20.7, SD: 5.3)
5ml Liquid Swallows	**Baseline**	10	7.7mm (5.3-9.4, SD: 1.1)	8mmHg (3.6-16.7, SD: 4)
	Head Turn Right	9	8.1mm (5.1-15.8, SD: 3.1)	1.5mmHg (-2.9-5.4, SD: 3.9)
	Head Turn Left	9	8.3mm (5.1-15.9, SD: 3.2)	4.2mmHg (-0.4-9.6, SD: 3.7)
	Chin Tuck	9	8.4mm (4.9-12.7, SD: 2.4)	7mmHg (4.2-12.5, SD: 3.5)
	Effortful Swallow	9	8.5mm (4.9 - 15.2, SD: 2.9)	3.4mmHg (- 4.7-10.8, SD: 4.7)
	Mendelsohn Manoeuvre	9	8.1mm (5.0- 14.7, SD:2.8)	5.2mmHg (2.7-11.5, SD: 3.9)
	Supraglottic Swallow	9	7.8mm (5-15.2, SD: 3)	2.7mmHg (-5.5-14.6, SD: 5.5)

Figure Legends

Figure 1. Current Evaluation of UES Opening

Figure 2. EndoFLIP® System

A) EndoFLIP®
B) FLIP balloon
C) FLIP balloon safely distended in UES during videofluoroscopy
D) Geometric profile of UES on EndoFLIP® screen.

Figure 3. UES Distensibility

Figure 4
UES Diameter and Intra-Balloon Pressure Changes During Swallowing in Four Healthy Subjects.

Figure 5
Geometric Profiles of UES on EndoFLIP® Screen Across Voluntary Manoeuvres in a Healthy Subject.