Endoluminal Functional Lumen Imaging Probe (EndoFLIP) in Challenging Esophageal Disorders

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Harvard Medical School
What is non-obstructive dysphagia?
Case #1: young man with dysphagia

What is a “functional lumen imaging probe?”
Case #1 wrap up

What are esophageal diseases that can be studied with EndoFLIP?
Achalasia
GERD
Eosinophilic esophagitis

Highlighting EndoFLIP, additional cases:
Case #2: young-ish man with dysphagia after Heller myotomy
Case #3: dysphagia not meeting Chicago classification criteria
Case #4: a possible complication of anti-reflux surgery?

Clinical pearls
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Clinical pearls
Swallowing and the esophagus:

- Measures approximately 20-22 cm in length
- Percentage of skeletal and smooth muscle varies based on location:
  - First 5% is composed almost exclusively of striated skeletal muscle (~1 cm distal to the UES/hypopharynx)
  - Middle 35-50% (next 7-11 cm) is mixed smooth and skeletal muscle (increasingly smooth distally)
  - Remaining 40-60% of the esophagus distally is entirely smooth muscle.
Swallowing and the esophagus:

Musculature of Esophagus

- Interior pharyngeal constrictor muscle
- Pharyngeal caphe
- Zone of sparse muscle fibers
- Cricopharyngeus muscle
- Part of inferior pharyngeal constrictor
- Main longitudinal muscle bundle
- Rounded and ventrally to partially encircles oropharyngeal surface of cricoid cartilage
- Accessory muscle bundle from posterior-lateral surface of cricoid cartilage
- Additional fibers from contralateral side of cricopharyngeus muscle
- Part of inferior pharyngeal constrictor
- Circular muscle layer with sparse longitudinal fibers
- Wedged area (lamina)
- Bare area on ventral surface of esophagus
- Lateral mass of longitudinal muscle
- Fibroelastic membranes with sparse muscle fibers
- Window cut in longitudinal muscle layer
- Circular muscle layer

www.pathologyoutlines.com
www.bcr.bio.umass.edu
Swallowing and the esophagus:

- The above muscles coordinate to allow for transit of a food bolus beyond the UES through the esophagus that while reliant on gravity, can function independently of gravity.
- The esophagus at rest should not have any spontaneous contractions, but when it does, it does so in a coordinated fashion called peristalsis.
  - **Primary** peristalsis
    - Initiated by swallowing; stimulus traverses the entire length of the esophagus
  - **Secondary** peristalsis
    - Focal contraction in response to local distention.
Swallowing and the lower esophagus:

- The **esophagogastric junction has 3 components**
  - The lower esophageal sphincter
  - The crural diaphragm
  - The gastric cardia
- The lower esophageal sphincter
  - 3-4 cm in length
  - Tonically contracted.
- Highest pressure is 1 to 1.5 cm proximal to the squamocolumnar junction to 2 cm distal to it.
- LES under the influence of excitatory ACh-sensitive neurons (causing contraction) and inhibitory nitric-oxide neurons (causing relaxation)
What to do with dysphagia?

• Dysphagia is the overlap between structural or neuromuscular disorders in the esophagus and pharynx.

• Dysphagia is likely due to a structural etiology (stricture, malignancy, eosinophilic esophagitis etc.) when there is an absence of symptoms with liquids or there is a predominance of complaints (including chest pain) with solid foods.

• In contrast, dysphagia is likely due to a neuromuscular disorder when there is presence of difficulty swallowing to BOTH solids and liquids.

• However, this is hardly absolute.
What to do with dysphagia?

- The prevalence of dysphagia in those over 50 years of age ranges from 16% to 22%.

- Although the vast majority of oropharyngeal dysphagia is due to neuromuscular disease, due to the treatability of structural disease of the esophagus, upper endoscopy is a reasonable first test for evaluating new-onset dysphagia.

- EGD has an estimated diagnostic yield of 54% in patients 40 years or older with symptoms of dysphagia, heartburn, odynophagia, and heartburn.

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**TABLE 2. Common etiologies of esophageal dysphagia**

<table>
<thead>
<tr>
<th>Common etiologies</th>
<th>Amenable to dilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign etiologies</td>
<td></td>
</tr>
<tr>
<td>Peptic stricture</td>
<td>Yes</td>
</tr>
<tr>
<td>Schatzki ring</td>
<td>Yes</td>
</tr>
<tr>
<td>Esophageal web</td>
<td>Yes</td>
</tr>
<tr>
<td>Eosinophilic esophagitis</td>
<td>Yes</td>
</tr>
<tr>
<td>Caustic injury</td>
<td>Yes</td>
</tr>
<tr>
<td>Anastomotic stricture</td>
<td>Yes</td>
</tr>
<tr>
<td>Radiation injury</td>
<td>Yes</td>
</tr>
<tr>
<td>Pill-induced stricture</td>
<td>Yes</td>
</tr>
<tr>
<td>Post-endoscopic therapy stricture</td>
<td>Yes</td>
</tr>
<tr>
<td>Congenital esophageal anomalies (tracheoesophageal fistula)</td>
<td>Yes</td>
</tr>
<tr>
<td>Cricopharyngeal bar</td>
<td>Yes</td>
</tr>
<tr>
<td>Malignant etiologies</td>
<td></td>
</tr>
<tr>
<td>Esophageal adenocarcinoma</td>
<td>Yes</td>
</tr>
<tr>
<td>Esophageal squamous cell carcinoma</td>
<td>Yes</td>
</tr>
<tr>
<td>Pseudoachalasia</td>
<td>Yes</td>
</tr>
<tr>
<td>Extrinsic compression</td>
<td>No</td>
</tr>
<tr>
<td>Motility disorders</td>
<td></td>
</tr>
<tr>
<td>Achalasia</td>
<td>Yes</td>
</tr>
<tr>
<td>Diffuse esophageal spasm</td>
<td>No</td>
</tr>
<tr>
<td>Hypomotility (secondary to connective tissue disorders)</td>
<td>No</td>
</tr>
</tbody>
</table>

Sleisenger & Fordtran's 10th edition
Endoscopy for dysphagia GIE
2014

A Teaching Affiliate
of Harvard Medical School
What if the EGD is negative/ not available?

- A reasonable next step in this instance would be **contrast imaging** via a modified barium swallow study or barium esophagram.

- There are notable advantages to contrast imaging *versus* endoscopy:
  - They allow for a functional evaluation of the patient’s ability to tolerate a food bolus.
  - Can assess for delays in initiating pharyngeal swallowing.
  - Can detect aspiration events.
  - Can identify remaining residue in the pharynx which would normally be cleared after the pharyngeal stripping wave.
  - Can assess for peristalsis (with an over 90% specificity).
  - Can assess the EGJ complex’s response to a food bolus.
When endoscopy and contrast imaging fail to give a clear diagnosis?

Sleisenger & Fordtran's 10th edition
High resolution manometry 101:

- **Integrated relaxation pressure (IRP)** is used to evaluate EGJ complex relaxation.
  - Mean of the 4-second maximal relaxation in the 10-second deglutitive window (beginning with swallowing). It is device specific.

- **Distal contractile integral (DCI)** is used to assess contractile vigor.

- Contractile deceleration point (CDP) represents the inflection point at the 30 mmHg isobaric contour, demarcating esophageal peristalsis from emptying.

- **Distal latency (DL)** represents the integrity of the of inhibitory pathways preceding esophageal contractions, measured as the interval from UES relaxation to the CDP. Smaller value, worse impairment.
Case #1: young man with dysphagia

- **CC:** dysphagia x 5 years

- **HPI:** Patient is a 21-year-old man who presents for evaluation.

- He had an **abnormal** barium esophagram and in Colorado had **undergone 3 EGD dilations**, the most recent one occurring 4 months prior to presentation with a Maloney 58 French dilator.

- **Transient** improvement with each dilation.
Case #1: young man with dysphagia

- Prior to his most recent dilation, he had **lost 60 pounds**, of which he had gained back 20 pounds upon consultation.

- Reported post-dilation esophagram with **decrease primary peristalsis**, esophageal dilation, and **tight narrowing at GEJ**. CT with proximal esophageal **air-fluid level**, and **multiple diffuse small lung infiltrates**, largest = 1.3 cm

- Upon review of systems, also complained of **cough**.

- Family history remarkable for a grandmother who had dysphagia and likely had esophageal dilations.
Case #1: young man with dysphagia

What are your next steps for diagnostic work-up/ therapeutic intervention?
Case #1: young man with dysphagia

- Mean integrated relaxation pressure (IRP): 13.6 mmHg
- Mean basal LES pressure: 22.6 mmHg
- Normal LES relaxation with 0% peristaltic swallows, 100% ineffective swallows, (100% failed swallows, 0% weak swallows), and 0% fragmented contractions)
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Clinical pearls
What is EndoFLIP?

*EndoFlip Equipment:* The EndoFLIP® system comprises a measuring system and a single use catheter to assist in measuring dimensions and distensibility within the esophagus and stomach. The system uses the impedance planimetry technique to characterize the geometry of the lumen.

![EndoFLIP® system](image1)

![Distal end of EndoFLIP® Balloon Catheter](image2)

*Figure 1: EndoFLIP® system*  
*Figure 2: Distal end of EndoFLIP® Balloon Catheter*
What is EndoFLIP?
What is EndoFLIP?

- FDA approved tool utilized to measure simultaneous pressure and diameter to both diagnose and manage various upper gastrointestinal disorders.
- Also approved to guide therapy during bariatric procedures and specialized esophageal surgery.
- Commercially available since 2009, but limited penetrance outside of specialized centers.
  - primarily due to a paucity of data supporting its utility in general practice.
- Data is accumulating that is providing guidance regarding emerging applications in the evaluation and management of foregut disorders.

Hirano et al CGH 2017
What is EndoFLIP?

- The probe is a 240-mm long, 3-mm outer diameter catheter with a balloon at the distal end of varying sizes (6 cm to 16-cm).
  - The catheter contains 16 paired impedance planimetry electrodes within the balloon spaced at various intervals ranging from 4mm to 1 cm based on the bag configuration and length.
  - An infinitely compliant balloon of varying diameters based on the assessment required is filled with a conductive fluid from an 80 ml syringe
What is EndoFLIP?

- Excitation electrodes at either end of the balloon emit a continuous low electric current and the voltage is measured across the paired impedance planimetry electrodes to **obtain measurement of cross sectional area (CSA) and volume** at intervals based on excitation electrode spacing.

- A solid-state pressure transducer is located at the distal end of the bag and thus, a simultaneous **measures of pressure is made and an assessment of distensibility of the esophageal body and/or EGJ can be performed.**
What is EndoFLIP?

- The FLIP is placed into the esophagus either trans-orally or trans-nasally in a sedated or awake patient.
- The FLIP is positioned within the esophagus by identifying the waist-like constriction of the esophagogastric junction on the real-time, 3 dimensional (3-D) geometric display at a low fill volumes (typically 20–30ml)
- During FLIP assessment, measurements of 16 CSA and pressure are simultaneously measured using a 10-Hz sampling rate.
- The distensibility index (DI) is the typical measure of sphincter distensibility and is calculated by dividing the median narrowest CSA (within the anatomical zone of interest) by the median intra-bag pressure over a set timeframe
  - Dynamic (respiratory and vascular artifacts and esophageal contraction)

Hirano et al CGH 2017
Normal EndoFLIP
Achalasia EndoFLIP

Hirano et al. CGH 2017

Massachusetts General Hospital
Digestive Healthcare Center
**Case #1: young man with dysphagia**

<table>
<thead>
<tr>
<th>Volume</th>
<th>DI</th>
<th>CSA</th>
<th>Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>40mL</td>
<td>2.6</td>
<td>30</td>
<td>6.1</td>
</tr>
<tr>
<td>50mL</td>
<td>2.6</td>
<td>39</td>
<td>7.3</td>
</tr>
<tr>
<td>60mL</td>
<td>3.7</td>
<td>67</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Smeets *et al* 2015 Esophagogastric junction distensibility in the management of achalasia patients: relation to treatment outcome. NGM
Case #1: young man with dysphagia

Wrap-up: Patient is undergoing planning for **Heller myotomy with fundoplication** despite the normal IRP
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Clinical pearls
Distensibility of the esophagogastric junction assessed with the functional lumen imaging probe (FLIP™) in achalasia patients

J. E. PANDOLFINO, A. DE RUIGH, F. NICODÈME, Y. XIAO, L. BORIS & F. J. KAHRLAS

Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA
EndoFLIP in Achalasia

- Fifty-four patients [age (19–80) years, 29 men] were studied.
- Prospectively recruited from the Esophageal Center at Northwestern based on esophageal symptoms suggestive of achalasia and previous evaluation confirming achalasia on HRM.
- Two cohorts were recruited: Group A [no achalasia treatment] and Group B [patients after treatment with pneumatic dilation (n = 17), Heller myotomy with partial fundoplication (n = 10) or per-oral esophageal myotomy (n = 4)].
- Every patient also underwent manometry, timed barium esophagram, and endoscopy as part of their clinical evaluation within 1 month of the FLIP study. They filled out an Eckardt Score as well (good response < 3, bad response if > 3)
- Data from previously studied asymptomatic controls were utilized as a healthy control group for EGJ distensibility.

Pandolfino et al NGM 2013
## Table 2 EGJ-DI during volume distentions – median [5th–95th]

<table>
<thead>
<tr>
<th>FLIP™ bag volume (mL)</th>
<th>Control subjects</th>
<th>Untreated achalasia</th>
<th>Achalasia, good treatment response</th>
<th>Achalasia, poor treatment response</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>4.2 [0.3–7.1]</td>
<td>1.1 [0.9–1.6]</td>
<td>1.8 [1.2–2.2]</td>
<td>1.4 [1–2.2]</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>30</td>
<td>5.1 [0.8–21.7]</td>
<td>1 [0.8–1.2]</td>
<td>2.5 [1.3–3.4]</td>
<td>1.1 [0.8–2.6]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>40</td>
<td>8.2 [1.7–18.7]</td>
<td>0.7 [0.5–1.1]</td>
<td>3.4 [2.2–4.9]</td>
<td>1.5 [0.6–2.8]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
EndoFLIP in Achalasia

Pandolfino et al. NGM 2013
Feasibility of esophagogastric junction distensibility measurement during Nissen fundoplication

A. Ilczyszyn, A. J. Botha

Department of Upper GI Surgery, Guys’ and St Thomas’ NHS Foundation Trust, St Thomas’ Hospital, London, UK
Seventeen patients with GERD were managed in a standardized manner consisting of preoperative assessment with symptom scoring, endoscopy, 24 hours pH studies, and manometry. Patients then underwent laparoscopic Nissen fundoplication with intraoperative distensibility measurement using an EndoFLIP EF-325 functional luminal imaging probe.

Measurement time points were (1) initially after induction of anesthesia, (2) after pneumoperitoneum, (3) after hiatal mobilization, (4) after hiatal repair, (5) after fundoplication, (6) and finally pre-extubation.
EndoFLIP in fundoplications

Ilczyszyn and Botha Dis Esoph 2013
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Clinical pearls
Case #2: young-ish man with dysphagia

- **CC:** *dysphagia* status-post Heller myotomy and fundoplication

- **HPI:** 38-year-old man who had a Heller myotomy in 2015 for *type 1 achalasia*, paired with a Toupet fundoplication.

- He has been complaining recently of *worsening dysphagia* complaints. Of note, he had delayed myotomy for several years but eventually agreed.

- Repeat EGD Summer 2018 without any obstructive lesion in the esophagus.

- He underwent esophageal manometry and timed barium esophagram.
Case #2: young-ish man with dysphagia
Case #2: young-ish man with dysphagia

- Repeat manometry 6 months ago showed an **IRP of 1.4 mmHg** as well as 100% failed swallows consistent with treated type 1 achalasia.

- Timed barium esophagram revealed a dilated and tortuous esophagus compatible with **abnormal retention of contrast at 1 minute and approximately 50% clearing at 5 minutes**. These findings have improved from 2016 study, at which time only approximately 25% cleared by 5 minutes.
Case #2: young-ish man with dysphagia

40 cc: diameter = 5.0 CSA = 19 **Distensibility Index** = 1.2 Pressure = 15.3
50 cc: diameter = 7.8 CSA = 52 **Distensibility Index** = 3.0 Pressure = 19.2
60 cc: diameter = 12 CSA = 115 **Distensibility Index** = 4.5 Pressure = 28.6
Case #3: dysphagia outside of Chicago

- **CC:** dysphagia with an abnormal manometry

- **HPI:** 64-year-old man presents for evaluation of difficulty swallowing for several years after having manometry **not meeting strict criteria by the Chicago classification.**

- Symptoms started several years ago. In the beginning, sudden onset on a restaurant in Florida. Episodes occurred once every few months sporadically.

- An esophagram showed **prompt passage of contrast** after 3 dilations, but **previously had shown spasms and delay** in contrast passage before.
Case #3: dysphagia outside of Chicago

- **Mixed motility disorder** with diffuse esophageal spasm and panesophageal pressurization demonstrated on majority of swallows.
- 80% of swallows with failed peristalsis due to panesophageal pressurization across a relaxed LES.
Clinical pearls: esophageal EndoFLIP Imaging was performed using EndoFLIP.

<table>
<thead>
<tr>
<th>Volume (mL)</th>
<th>Diameter</th>
<th>CSA</th>
<th>DI</th>
<th>Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>4.8</td>
<td>18</td>
<td>1.1</td>
<td>15</td>
</tr>
<tr>
<td>50</td>
<td>4.8</td>
<td>18</td>
<td>0.8</td>
<td>41</td>
</tr>
<tr>
<td>60</td>
<td>4.8</td>
<td>18</td>
<td>0.4</td>
<td>51</td>
</tr>
<tr>
<td>70</td>
<td>6.0</td>
<td>29</td>
<td>0.4</td>
<td>78</td>
</tr>
</tbody>
</table>

Case #3: dysphagia outside of Chicago
Case #4: possible surgical complication?

- **CC:** *dysphagia* status-post fundoplication for GERD

- **HPI:** 58-year-old woman s/p laparoscopic paraesophageal hernia repair with fundoplication who has had *post operative dysphagia* to solids and liquids, chronic cough, chest pressure, throat clearing, globus and upper abdominal pain.

- Consultation requested to see if the patient required a re-do of her fundoplication.

- Barium esophagram with prompt contrast clearance. High resolution manometry was ordered.
Case #4: possible surgical complication?

- Mean integrated relaxation pressure (IRP): 27.4 mmHg
- Mean basal LES pressure: 43.5 mmHg
- Consistent with EGJ outflow obstruction
Case #4: possible surgical complication?

Imaging was performed using EndoFLIP.

- **40 mL**: Diameter: 11  
  CSA: 40  
  DI: 2  
  Pressure: 30

- **50 mL**: Diameter: 13  
  CSA: 130  
  DI: 4  
  Pressure: 35

- **60 mL**: Diameter: 15  
  CSA: 140  
  DI: 3.5  
  Pressure: 52
**Best Practice Advice 1:** Clinicians should not make a diagnosis or treatment decision based on functional lumen imaging probe (FLIP) assessment alone.

**Best Practice Advice 2:** FLIP assessment is a complementary tool to assess esophagogastric junction opening dynamics and the stiffness of the esophageal wall.

**Best Practice Advice 3:** Utilization should follow distinct protocols and analysis paradigms based on the disease state of interest.

**Best Practice Advice 4:** Clinicians should not utilize FLIP in routine diagnostic assessments of gastroesophageal reflux disease.

**Best Practice Advice 5:** FLIP should not be used to diagnose eosinophilic esophagitis but may have a role in severity assessment and therapeutic monitoring.
Hirano et al 2017 Functional Lumen Imaging Probe for the Management of Esophageal Disorders: Expert Review From the Clinical Practice Updates Committee of the AGA Institute. CGH
Pandolfino et al 2013. Distensibility of the esophagogastric junction assessed with the functional lumen imaging probe (FLIPTM) in achalasia patients. NGM
Smeets et al 2015 Esophagogastric junction distensibility in the management of achalasia patients: relation to treatment outcome. NGM
Kwiatek et al 2010. Esophagogastric junction distensibility assessed with an endoscopic functional luminal imaging probe (EndoFLIP). GIE
Ponds et al 2017. Esophagogastric junction distensibility identifies achalasia subgroup with manometrically normal esophagogastric junction relaxation. NGM
Familiari et al. EndoFLIP system for the intraoperative evaluation of peroral endoscopic myotomy. UEGJ
Ilczyszyn and Botha 2013. Feasibility of esophagogastric junction distensibility measurement during Nissen fundoplication. Dis Esoph