HHS Public Access

Author manuscript

Gastroenterol Clin North Am. Author manuscript; available in PMC 2021 September 01.

Published in final edited form as:

Gastroenterol Clin North Am. 2020 September ; 49(3): 427–435. doi:10.1016/j.gtc.2020.04.002.

EndoFLIP in the esophagus: assessing sphincter function, wall stiffness, and motility to guide treatment

Erica N. Donnan, MD, **John E Pandolfino, MD, MSCI**

Division of Gastroenterology and Hepatology, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, NMH/Arkes Family Pavilion Suite 1400, 676 N Saint Clair, Chicago, Illinois 60611

Keywords

impedance; achalasia; dysphagia; FLIP; EndoFLIP; gastroesophageal reflux

Introduction

The techniques used to measure esophageal and sphincter physiology have evolved over time with high-resolution manometry and the functional luminal imaging probe (FLIP) taking center stage over the past 10 years. Currently high-resolution manometry in combination with the Chicago Classification v3.0 is the “Gold Standard” for the clinical assessment of esophageal motility disorders.[1] However, a growing body of literature surrounding the use of the functional luminal imaging probe has demonstrated its clinical utility as both a diagnostic tool and as a device which can be used to guide and measure response to therapy.

The FLIP provides a three-dimensional image of the esophageal lumen through use of high-resolution impedance planimetry to measure pressure changes, diameter and volume. By measuring distensibility, the FLIP can measure esophageal wall stiffness and the dynamics of esophagagogastric junction (EGJ) opening.[2] The Esophagogastric Junction-Distensibility Index (EGJ-DI) is the measure of sphincter distensibility and is derived by dividing the median narrowest cross-sectional area by the median intra-balloon pressure over a set timeframe. The use of the EGJ-DI combined with contraction patterns, known as FLIP panometry, allows for the classification of esophageal motility.[3]

There is now published normative data from healthy control patients which will allow the FLIP to be applied to clinical practice.[4] In 2017 the AGA Institute’s Clinical Practice

corresponding author, Phone: 312 695 0929, erica.donnan@northwestern.edu.

Disclosure statement: JEP holds shared intellectual property rights and ownership surrounding FLIP panometry systems, methods and apparatus with Medtronic Inc. Other JEP disclosures Crospon, Inc (stock options), Given Imaging (Consultant, Grant, Speaking), Sandhill Scientific (Consulting, Speaking), Takeda (Speaking), Astra Zeneca (Speaking), Medtronic (Speaking. Consulting), Torax (Speaking, Consulting), Ironwood (Consulting), Impleo (Grant). END has nothing to disclose.

Updates Committee published an Expert Review of FLIP. The paper summarized the best practice advice recommending that while the FLIP should not be used in isolation to make diagnostic or treatment decisions, it is a complementary tool to assess EGJ opening dynamics and stiffness of the esophageal wall.[5] The purpose of this review article is to summarize the use of the FLIP in assessing motility, the sphincter function and wall stiffness to guide treatments.

The FLIP catheter, study protocol, data analysis

The FLIP is comprised of a catheter with a distal overlying balloon. Within the balloon there are 16 paired impedance planimetry electrodes and a solid-state pressure transducer located distally. There is a continuous low electric current that is emitted by excitation electrodes located on both ends of the balloon. The balloon is inflated with saline enabling the measurement of voltage across the impedance planimetry electrodes. This allows for the measurement of the luminal cross sectional area.

The FLIP is typically placed in a sedated patient at the time of endoscopy and can be placed and performed in less than 5 minutes.[6] The FLIP is placed transorally and is positioned within the esophagus through the identification of the waist on a display figure with 20 mL of saline in the balloon. The catheter will often move during the study as the esophagus contracts-using the waist on the display figure allows for readjustment of the balloon during the study. Once the catheter is at the correct position, the balloon is distended typically step-wise in 10 mL increments up to 70 mL.

There was previously a delay between the upper endoscopy and the interpretation of FLIP panometry as the FLIP required the use of a customized analysis program prior to interpretation. However, the manufacturer [Medtronic Inc, Shoreview MN] has created FLIP 2.0 with a screen that displays 40 seconds of continuous FLIP topography during the time of the endoscopy so that now the operator can interpret the measurements in real time using FLIP panometry (see Figure 1). Carlson et al recently demonstrated this in a prospective multi-centered study with excellent agreement between real-time and post-hoc FLIP panometry interpretation of abnormal motility.[7]

Assessing Motility

Repetitive Antegrade Contractions, Repetitive Retrograde Contractions, Disordered Contractility

When the esophagus is distended by the FLIP, contractions are induced that are currently subdivided into three categories-repetitive antegrade contractions (RACs), repetitive retrograde contractions (RRCs) and lastly diminished-disordered contractile response (DDCR))(see Figure 2).[3,8,9] FLIP panometry combines the EGJ-DI along with the contractility pattern to categorize the esophageal motility. The classification scheme has been previously published and is initially designated by the presence or absence of EGJ outflow obstruction defined by an abnormal EGJ-DI and then the contractility pattern.[3] Recently published data from 20 asymptomatic healthy control patients found that RACs are a normal response to sustained esophageal distension.[4]

Assessing the Sphincter Function

Lower Esophageal Sphincter

Gastroesophageal Reflux Disease—It is hypothesized that increased EGJ distensibility and dimension should increase the volume of reflux in patients with gastroesophageal reflux disease (GERD). This is based on Poiseuille's Law of Flow which states that flow rate of a liquid through a tube is directly proportional to the fourth power of the radius of the tube and inversely related to the length and viscosity of the tube. The EGJ of GERD patients with a hiatal hernia was found to be shorter and more distensible than normal subjects in a study that combined concurrent esophageal manometry, fluoroscopy and stepwise controlled barostatic distention of the EGJ.[10] The majority of research involving GERD and the FLIP has focused on the EGJ-DI, however the results have shown conflicting data. The best practice statement from the AGA Institute's Clinical Practice Updates Committee Expert Review recommends against utilizing the FLIP for routine GERD management.[5]

In a study using the FLIP to evaluate patients with hiatal hernias and Barrett's esophagus compared to controls, the lower esophageal sphincter in patients with a hiatal hernia had a lower pressure and was more distensible than the EGJ in controls.[11] In a different study the EGJ is more distensible in reflux patients than in control subjects.[12] However, when the FLIP was used to evaluate patients with GERD symptoms in addition to 48-hour wireless esophageal pH monitoring compared to asymptomatic control subjects, the patients with GERD were found to have a lower EGJ-DI and the EGJ-DI was not different between normal or abnormal esophageal acid exposure.[13] Another study evaluated 25 patients undergoing reflux testing for suspected GERD with the FLIP and with ambulatory wireless esophageal pH testing off of proton-pump inhibitors.[14] The EGJ-DI did not differ between abnormal acid exposure time and normal acid exposure time. They did however find that patients with RACs had a lower total acid exposure time, supporting the importance of secondary peristalsis for clearing acid from the esophagus.[14]

The use of the FLIP for preoperative assessment and intraoperative use has been studied for GERD procedures. Preoperative EGJ-DI was not found to be predictive of clinical outcomes after transoral incisionless fundoplication.[15] In one study fundoplication did reduce distensibility to normal levels.[16] The goal of using intraoperative FLIP is to tailor the tightness of the fundoplication to the individual. Intraoperative use of the FLIP to measure distensibility during a laparoscopic Nissen fundoplication has been found to be feasible and in one instance changed intraoperative management. [17] There is a published case report of using the FLIP to replace the rigid bougie commonly used during a Nissen and the authors commented that the FLIP intraoperatively was useful to evaluate the orientation and the position of the Nissen.[18] It has not been studied if intraoperative use of FLIP for Nissen fundoplication can change outcomes.

The conflicting data about GERD and the EGJ-DI may reflect that the EGJ-DI is not the most important measurement in assessing reflux as the opening dimensions and pressure gradient for reflux are much lower than those produced during swallowing. Future studies in

GERD should assess the rate of opening and the yield pressure for opening as the dynamic relationship between opening at lower pressures may be more relevant.

Achalasia

The hallmark feature of achalasia is the failure of the lower esophageal sphincter to relax. The FLIP is ideally suited to assess the lower esophageal sphincter and has thus proven to be a useful tool in the diagnosis and management of achalasia. FLIP topography is a sensitive marker of achalasia, it has been found to identify abnormalities in esophageal motility including 100 % of patients with achalasia in several studies.[3,7]

Focusing on assessment of the lower esophageal sphincter through the EGJ-DI and the EGJ cross sectional area, the FLIP can be utilized during the treatment of achalasia. Intraoperative FLIP has been studied during per-oral endoscopic myotomy (POEM) for achalasia with the findings that EGJ cross-sectional area correlates with clinical response in addition to post-procedure reflux.[19] Intraoperative FLIP has been utilized for patients undergoing surgical myotomy to evaluate the EGJ cross-sectional area, with the finding that surgical myotomy significantly decreases contractile vigor.[20]

The EGJ-DI has been found to be predictive of immediate clinical response to pneumatic dilation in achalasia. A prospective study measured the EGJ-DI immediately before and after pneumatic dilation in patients with idiopathic achalasia and found that an incremental increase of the EGJ distensibility index of >1.8 mm^2/mm Hg after the pneumatic dilation was able to accurately predict clinical response.[21] With this information physicians can provide appropriate follow up and schedule anticipated needed procedures at the time of the initial pneumatic dilation. When the DI was prospectively evaluated in patients with achalasia post treatment, it was found to be the single most useful measure of EGJ opening.[22]

The FLIP can be helpful clinically to diagnose achalasia in patients with features of achalasia that do not meet the manometric criteria for achalasia. One study evaluated a subgroup of patients with clinical and radiological features of achalasia but did not have an IRP >15 as required by the Chicago Classification for diagnosis. These patients were found to have decreased EGJ distensibility and they symptomatically improved after treatment for achalasia.[23]

Esophagogastric Junction Outflow Obstruction

EGJ outflow obstruction as a diagnosis under the Chicago Classification of esophageal motility disorders on high-resolution manometry is a challenging category to diagnose and treat as it represents a heterogeneous group of diseases including mechanical obstruction, evolving achalasia or an artifact of the manometry catheter.[24] The FLIP can help confirm a true obstruction. We recommend utilizing the FLIP for the investigation of non-obstructive dysphagia (see Figure 3).[3]

Upper esophageal sphincter

The upper esophageal sphincter (UES) is essential for oropharyngeal swallowing and is comprised of the cricopharyngeus muscle, the proximal cervical esophagus and the inferior pharyngeal constrictor muscle. The UES is an interesting area of potential future FLIP application. The current methods to assess the UES includes video fluoroscopy, direct visualization with a nasopharyngeal scope, and pharyngeal manometry. The FLIP has been shown to be feasible and safe to evaluate the distensibility of the UES in post-laryngectomy patients.[25] Additionally, the FLIP has been used to measure upper sphincter distensibility and opening patterns during swallowing in healthy control subjects.[23] More studies are required for potential clinical application of the FLIP in the evaluation of the UES.

Assessing Wall Stiffness

Eosinophilic Esophagitis

Eosinophilic esophagitis (EoE) is a chronic immune mediated disease of the esophagus with chronic inflammation that lead to fibrosis of the esophageal lumen resulting in esophageal narrowing. Esophageal symptoms of EoE include dysphagia, regurgitation, chest pain and food impactions. Esophageal biopsies are histologically characterized by increased eosinophils.[26] The FLIP can be utilized in EoE to assess esophageal narrowing and the mechanical characteristics of the esophageal body. This includes measuring esophageal remodeling from fibrosis. The distensibility plateau can be identified through measuring the narrowest esophageal body cross-sectional area and the corresponding intra-balloon pressure during volume distension (see Figure 4). Compared to control patients, EoE patients have decreased compliance of the esophageal body.[27] Decreased distensibility using the FLIP has been shown in adults with EoE and is a risk factor for severity of rings and strictures seen endoscopically, need for dilation, and food impaction.[28] The FLIP may be superior to current practices of monitoring disease activity through upper endoscopy with biopsies as sampling may be inconsistent. Esophageal fibrosis measured endoscopically has been found to be inaccurate compared to fluoroscopy.[29]

The FLIP was recently studied in a pediatric population by Menard-Katcher et al and they found that esophageal distensibility is decreased in children with EoE compared to control and this corresponded to a 2 mm difference in esophageal caliber.[30] Distensibility in patients with EoE was negatively correlated with eosinophil density and children without EoE had increasing distensibility with age which was not found in the children with EoE. This points to esophageal remodeling results in decreased distensibility in children with EoE.

Summary/Discussion

The FLIP has demonstrated its clinical utility as both a diagnostic tool and a tool to guide and measure treatment response. With published normative data from healthy control patients and real-time interpretation of FLIP panometry during the endoscopy now available, FLIP is poised to become the initial test for the evaluation of dysphagia.

References

1. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015;27(2):160–174. [PubMed: 25469569]
2. McMahon BP, Frokjaer JB, Liao D, Kunwald P, Drewes AM, Gregersen H. A new technique for evaluating sphincter function in visceral organs: application of the functional lumen imaging probe (FLIP) for the evaluation of the oesophago-gastric junction. Physiol Meas. 2005;26(5):823–836. [PubMed: 16088071]
3. Carlson DA, Kahrilas PJ, Lin Z, et al. Evaluation of Esophageal Motility Utilizing the Functional Lumen Imaging Probe. Am J Gastroenterol. 2016;111(12):1726–1735. [PubMed: 27725650]
4. Carlson DA, Kou W, Lin Z, et al. Normal Values of Esophageal Distensibility and Distension-Induced Contractility Measured by Functional Luminal Imaging Probe Panometry. Clin Gastroenterol Hepatol. 2019;17(4):674–681 e671. [PubMed: 30081222]
5. Hirano I, Pandolfino JE, Boeckxstaens GE. Functional Lumen Imaging Probe for the Management of Esophageal Disorders: Expert Review From the Clinical Practice Updates Committee of the AGA Institute. Clin Gastroenterol Hepatol. 2017;15(3):325–334. [PubMed: 28212976]
6. Ahuja NK, Agnihotri A, Lynch KL, et al. Esophageal distensibility measurement: impact on clinical management and procedure length. Dis Esophagus. 2017;30(8):1–8.
7. Carlson DA, Gyawali CP, Kahrilas PJ, et al. Esophageal motility classification can be established at the time of endoscopy: a study evaluating real-time functional luminal imaging probe panometry. Gastrointest Endosc. 2019.
8. Carlson DA, Lin Z, Kahrilas PJ, et al. The Functional Lumen Imaging Probe Detects Esophageal Contractility Not Observed With Manometry in Patients With Achalasia. Gastroenterology. 2015;149(7):1742–1751. [PubMed: 26278501]
9. Carlson DA, Lin Z, Rogers MC, Lin CY, Kahrilas PJ, Pandolfino JE. Utilizing functional lumen imaging probe topography to evaluate esophageal contractility during volumetric distention: a pilot study. Neurogastroenterol Motil. 2015;27(7):981–989. [PubMed: 25898916]
10. Pandolfino JE, Shi G, Curry J, Joehl RJ, Brasseur JG, Kahrilas PJ. Esophagogastric junction distensibility: a factor contributing to sphincter incompetence. Am J Physiol Gastrointest Liver Physiol. 2002;282(6):G1052–1058. [PubMed: 12016131]
11. Lottrup C, McMahon BP, Ejstrud P, Ostapiuk MA, Funch-Jensen P, Drewes AM. Esophagogastric junction distensibility in hiatus hernia. Dis Esophagus. 2016;29(5):463–471. [PubMed: 25789842]
12. Kwiatek MA, Pandolfino JE, Hirano I, Kahrilas PJ. Esophagogastric junction distensibility assessed with an endoscopic functional luminal imaging probe (EndoFLIP). Gastrointest Endosc. 2010;72(2):272–278. [PubMed: 20541755]
13. Tucker E, Sweis R, Anggiansah A, et al. Measurement of esophago-gastric junction cross-sectional area and distensibility by an endolumenal functional lumen imaging probe for the diagnosis of gastro-esophageal reflux disease. Neurogastroenterol Motil. 2013;25(11):904–910. [PubMed: 23981175]
14. Carlson DA, Kathpalia P, Craft J, et al. The relationship between esophageal acid exposure and the esophageal response to volumetric distention. Neurogastroenterol Motil. 2018;30(3).
15. Smeets FG, Keszthelyi D, Bouvy ND, Masclee AA, Conchillo JM. Does Measurement of Esophagogastric Junction Distensibility by EndoFLIP Predict Therapy- responsiveness to Endoluminal Fundoplication in Patients With Gastroesophageal Reflux Disease? J Neurogastroenterol Motil. 2015;21(2):255–264. [PubMed: 25742904]
16. Kwiatek MA, Kahrilas K, Soper NJ, et al. Esophagogastric junction distensibility after fundoplication assessed with a novel functional luminal imaging probe. J Gastrointest Surg. 2010;14(2):268–276. [PubMed: 19911238]
17. Ilczyszyn A, Botha AJ. Feasibility of esophagogastric junction distensibility measurement during Nissen fundoplication. Dis Esophagus. 2014;27(7):637–644. [PubMed: 24033477]
18. Perretta S, Dallemagne B, McMahon B, D'Agostino J, Marescaux J. Video. Improving functional esophageal surgery with a "smart" bougie: Endoflip. Surg Endosc. 2011;25(9):3109. [PubMed: 21437739]

19. Ngamruengphong S, von Rahden BH, Filser J, et al. Intraoperative measurement of esophagogastric junction cross-sectional area by impedance planimetry correlates with clinical outcomes of peroral endoscopic myotomy for achalasia: a multicenter study. Surg Endosc. 2016;30(7):2886–2894. [PubMed: 26487227]
20. Campagna RAJ, Carlson DA, Hungness ES, et al. Intraoperative assessment of esophageal motility using FLIP during myotomy for achalasia. Surg Endosc. 2019.
21. Wu PI, Szczesniak MM, Craig PI, et al. Novel Intra-Procedural Distensibility Measurement Accurately Predicts Immediate Outcome of Pneumatic Dilatation for Idiopathic Achalasia. Am J Gastroenterol. 2018;113(2):205–212. [PubMed: 29206815]
22. Jain AS, Carlson DA, Triggs J, et al. Esophagogastric Junction Distensibility on Functional Lumen Imaging Probe Topography Predicts Treatment Response in Achalasia-Anatomy Matters! Am J Gastroenterol. 2019.
23. Ponds FA, Bredenoord AJ, Kessing BF, Smout AJ. Esophagogastric junction distensibility identifies achalasia subgroup with manometrically normal esophagogastric junction relaxation. Neurogastroenterol Motil. 2017;29(1).
24. Triggs JR, Carlson DA, Beveridge C, et al. Upright Integrated Relaxation Pressure Facilitates Characterization of Esophagogastric Junction Outflow Obstruction. Clin Gastroenterol Hepatol. 2019.
25. Regan J, Walshe M, Timon C, McMahon BP. 'Endoflip(R) evaluation of pharyngo-oesophageal segment tone and swallowing in a clinical population: a total laryngectomy case series'. Clin Otolaryngol. 2015;40(2):121–129. [PubMed: 25314664]
26. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). Am J Gastroenterol. 2013;108(5):679–692; quiz 693. [PubMed: 23567357]
27. Kwiatek MA, Hirano I, Kahrilas PJ, Rothe J, Luger D, Pandolfino JE. Mechanical properties of the esophagus in eosinophilic esophagitis. Gastroenterology. 2011;140(1):82–90. [PubMed: 20858491]
28. Nicodeme F, Hirano I, Chen J, et al. Esophageal distensibility as a measure of disease severity in patients with eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2013;11(9):1101–1107 e1101. [PubMed: 23591279]
29. Gentile N, Katzka D, Ravi K, et al. Oesophageal narrowing is common and frequently under-appreciated at endoscopy in patients with oesophageal eosinophilia. Aliment Pharmacol Ther. 2014;40(11–12):1333–1340. [PubMed: 25287184]
30. Menard-Katcher C, Benitez AJ, Pan Z, et al. Influence of Age and Eosinophilic Esophagitis on Esophageal Distensibility in a Pediatric Cohort. Am J Gastroenterol. 2017;112(9):1466–1473. [PubMed: 28508868]

Key points:

1. The FLIP has demonstrated its clinical utility as both a diagnostic tool and as a device which can be used to guide and measure response to therapy.
2. The FLIP can assess and guide treatments for esophageal disease states including gastroesophageal reflux disease, achalasia and eosinophilic esophagitis.
3. The FLIP can assess the sphincter function through the Esophagogastric Junction-Distensibility Index.
4. The wall stiffness can be measured by the FLIP by measuring esophageal narrowing and the mechanical characteristics of the esophageal body.
5. Motility can be classified by FLIP panometry- a combination of Esophagogastric Junction-Distensibility Index and contraction pattern at the time of upper endoscopy.

Synopsis

The functional luminal imaging probe (FLIP) uses high-resolution planimetry to provide a three-dimensional image of the esophageal lumen by measuring diameter, volume and pressure changes. A growing body of literature surrounding the use of the FLIP has demonstrated its clinical utility as both a diagnostic tool and as a device which can be used to guide and measure response to therapy. The FLIP can assess and guide treatments for esophageal disease states including gastroesophageal reflux disease (GERD), achalasia, and eosinophilic esophagitis. As further research is done, the FLIP may become the initial test for the patient with undifferentiated dysphagia at the time of their index endoscopy. The purpose of this review article is to summarize the use of the FLIP in assessing the sphincter function, wall stiffness and motility to guide treatments.

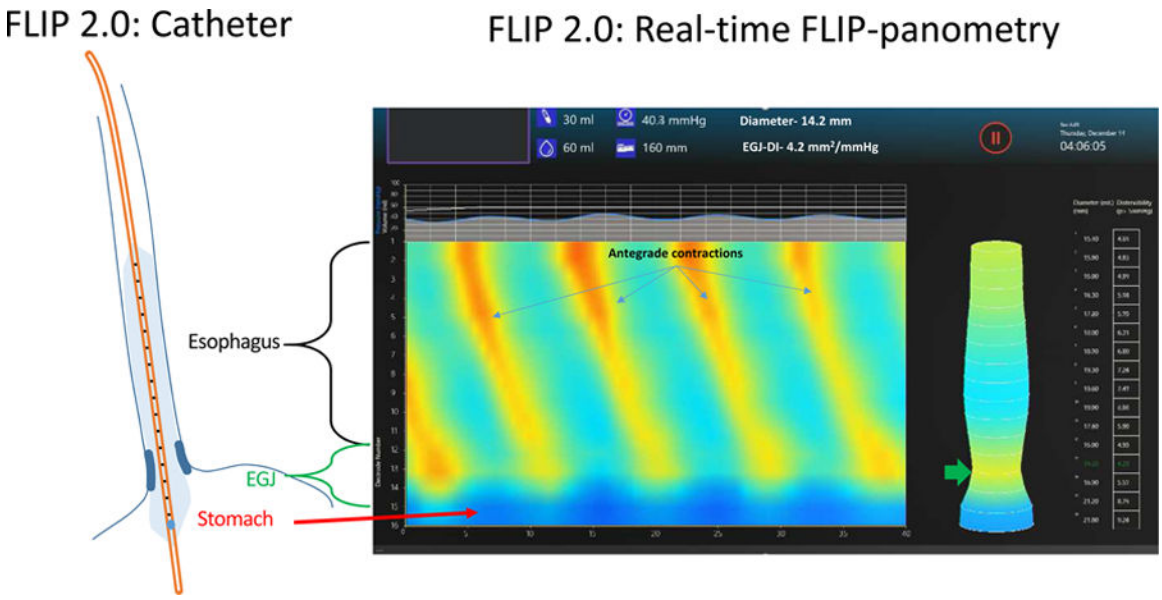

Figure 1:

Diagram of catheter and placement through the EGJ. The FLIP 2.0 display provides real-time measurement of the EGJ-DI that is measured as the narrowest CSA [green arrow] divided by the simultaneous pressure. The pattern represents a normal response to volumetric distention and is defined as repetitive antegrade contractions (RACs). *Courtesy of* the Esophageal Center at Northwestern, Chicago, IL.

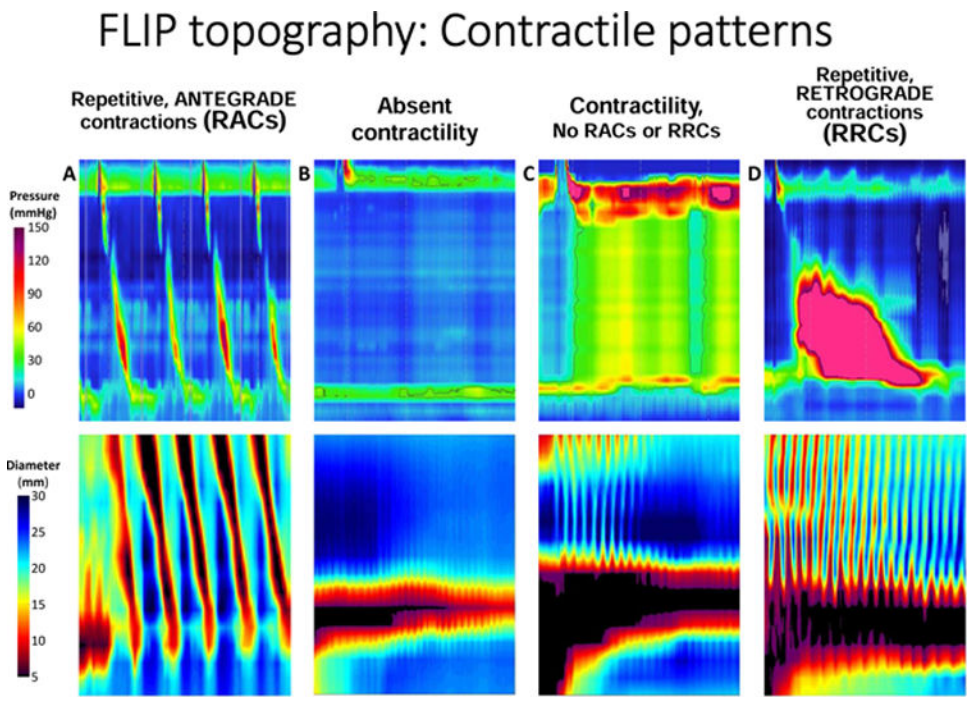

Figure 2:

Motility patterns in response to volumetric distention. The top panel is the high-resolution manometry image and the bottom panel is the FLIP topography image of the representative patient. Panel A is a normal subject with a RAC pattern. Panel B is a patient with Type I achalasia and the FLIP depicts an absent contractile response and a poorly relaxing sphincter. Panel C is type II achalasia and the FLIP suggests that there are disordered non-occluding contractions in the body of the esophagus and the sphincter does not open. Panel D is a patient with type III achalasia and the FLIP topography reveals an abnormal pattern where the contractions are retrograde and rapid in terms of the rate of contractions. *Courtesy of* the Esophageal Center at Northwestern, Chicago, IL.

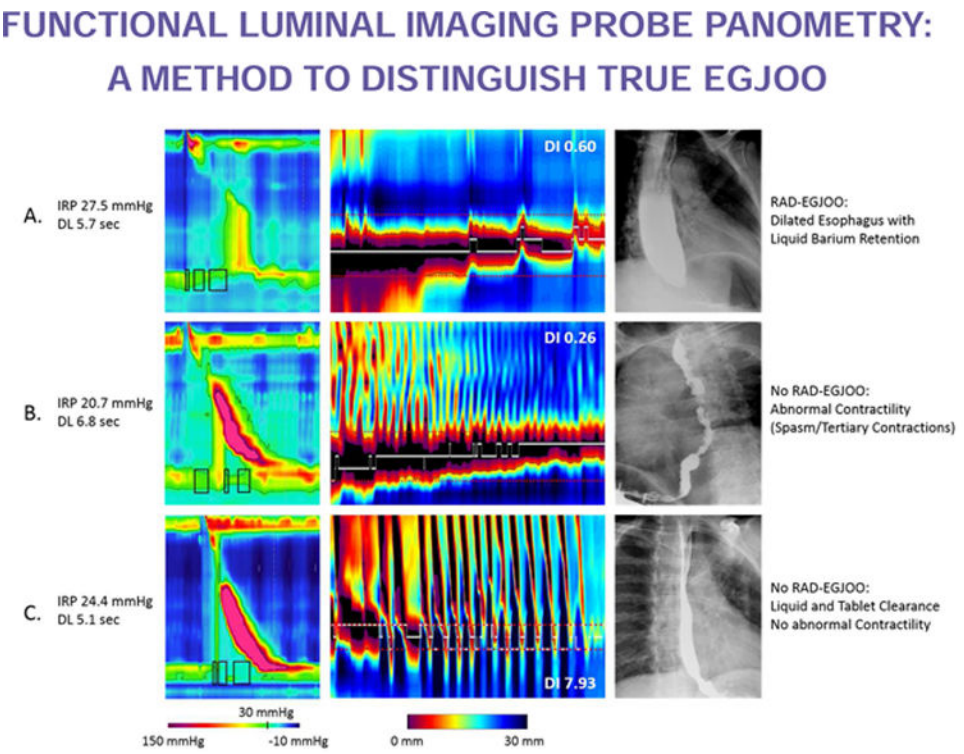

Figure 3:

Representative swallows on HRM (left panel), FLIP panometry (middle panel) and esophagram (right panel) for three patients diagnosed with EGJOO based on IRP > 15 mmHg. Patient A is a true-EGJOO (achalasia) with a FLIP DI <2 mm^2/mmHg. Patient B has a borderline abnormal manometry with some early compartmentalized pressurization during the swallow. However, the FLIP topography suggests a true EGJOO with FLIP DI <2 mm^2/mmHg and erratic contractions that are disordered and retrograde. This is more consistent with what is seen on the esophagram (rosary beads and corkscrew). Patient C is a false positive EGJOO on HRM as the FLIP reveals a normal RAC pattern and a normal EGJ-DI. The esophagram supports normal emptying.

Courtesy of the Esophageal Center at Northwestern, Chicago, IL.

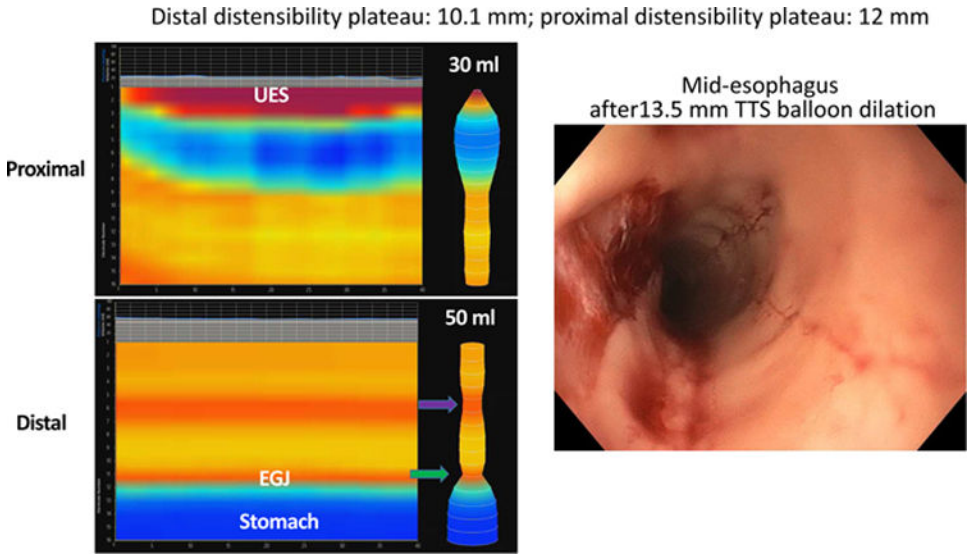

Figure 4:

Two representative FLIP 2.0 images of the distal and proximal esophagus. Note the sphincter landmark in each. They had a narrow caliber esophagus with a dominant EGJ stricture around 10 mm (green arrow) and another distal body stricture (purple arrow) around 12mm. Note the tear in the esophagus after a balloon dilation to 13.5 mm. *Courtesy of* the Esophageal Center at Northwestern, Chicago, IL.