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The Functional Lumen Imaging Probe Detects Esophageal Contractility Not Observed With Manometry in Patients With Achalasia

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BACKGROUND & AIMS: The functional lumen imaging probe (FLIP) could improve the characterization of achalasia subtypes by detecting nonocclusive esophageal contractions not observed with standard manometry. We aimed to evaluate esophageal contractions during volumetric distention in patients with achalasia using FLIP topography. **METHODS:** Fifty-one treatment-naive patients with achalasia, defined and subclassified by high-resolution esophageal pressure topography, and 10 asymptomatic individuals (controls) were evaluated with the FLIP during endoscopy. During stepwise distension, simultaneous intrabag pressures and 16 channels of cross-sectional areas were measured; data were exported to software that generated FLIP topography plots. Esophageal contractility was identified by noting periods of reduced luminal diameter. Esophageal contractions were characterized further by propagation direction, repetitiveness, and based on whether they were occluding or nonoccluding. **RESULTS:** Esophageal contractility was detected in all 10 controls: 8 of 10 had repetitive antegrade contractions and 9 of 10 had occluding contractions. Contractility was detected in 27% (4 of 15) of patients with type I achalasia and in 65% (18 of 26, including 9 with occluding contractions) of patients with type II achalasia. Contractility was detected in all 10 patients with type III achalasia; 8 of these patients had a pattern of contractility that was not observed in controls (repetitive retrograde contractions). **CONCLUSIONS:** Esophageal contractility not observed with manometry can be detected in patients with achalasia using FLIP topography. The presence and patterns of contractility detected with FLIP topography may represent variations in pathophysiology, such as mechanisms of panesophageal pressurization in patients with type II achalasia. These findings could have implications for additional subclassification to supplement prediction of the achalasia disease course.

Keywords: Esophagus; Motility; Peristalsis; EndoFLIP.

Achalasia is a primary esophageal motor disorder characterized by abnormal deglutitive lower esophageal sphincter (LES) relaxation and absent peristalsis, and is defined traditionally by evaluation with esophageal manometry.[1] Evaluation with high-resolution manometry (HRM) and esophageal pressure topography (EPT) have allowed further subclassification of achalasia based on the pressurization patterns observed in the esophageal body.[2] Type I (classic) achalasia is characterized by absent contractility, type II achalasia is characterized by panesophageal pressurization, and type III (spastic) achalasia is characterized by spastic (reduced latency) contractions.[2,3] Subclassification of achalasia has shown clinical utility in predicting symptomatic response to treatment (such as pneumatic dilation and Heller myotomy).[2,4–7]

Although absent peristalsis is a defining feature of achalasia, multiple studies have reported a return of peristalsis after treatment of achalasia.[8–10] Recovery of peristalsis has been attributed to removal of the distal esophagogastric junction (EGJ) obstruction, similar to animal models with imposed esophageal ligature or human beings with laparoscopic adjustable gastric banding.[11–13] However, an alternative hypothesis is that esophageal dilatation, common in achalasia, impedes contact of the esophageal wall with the manometry catheter to induce a measurable pressure signal and subsequent detection of esophageal contractions and peristalsis. In addition, panesophageal pressurization, the defining feature of type II achalasia, may obscure manometric detection of esophageal contractions. Longitudinal muscle has been implicated as the causal mechanism of common cavity pressurization and esophageal emptying in type II achalasia based primarily on an elegant ultrasound study of 7 patients with type II achalasia.[14] However, we have observed contractile activity of the esophagus during endoscopy in some patients with types I and II achalasia during endoscopy and suspect that this may be an additional mechanism of panesophageal pressurization.

The functional lumen imaging probe (FLIP) may offer a unique method to evaluate esophageal contractility in achalasia. The FLIP is a commercially available device (EndoFLIP; Crospon, Inc, Galway, Ireland) that uses multiple, closely spaced impedance planimetry channels located within a distensible bag to simultaneously measure luminal diameters and intrabag pressure during controlled

Abbreviations used in this paper: **CSA, cross-sectional area; DI, distensibility index; EGJ, esophagogastric junction; EPT, esophageal pressure topography; FLIP, functional lumen imaging probe; HRM, high-resolution manometry; IQR, interquartile range; LES, lower esophageal sphincter; RAC, repetitive antegrade contraction; RRC, repetitive retrograde contraction.**

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volumetric distension.[15] Although the FLIP has been used primarily in achalasia for the evaluation of EGJ distensibility,[16,17] we recently described a novel methodology to assess contractility in the esophageal body of asymptomatic controls: FLIP topography.[18] By positioning the FLIP catheter to span the distal esophagus and incorporating novel software programs to interpolate the multiple luminal diameter measurements, a FLIP topography plot can be generated to visualize esophageal body contractility with concurrent assessment of EGJ distensibility.[19]

Because the FLIP catheter bag distends within the esophageal lumen and can detect contractions by sequenced changes in luminal diameters, we hypothesized that application of FLIP topography may offer a method to detect nonocclusive esophageal contractions in patients with achalasia. The aim of this study was to use FLIP topography in patients with achalasia to define patterns of esophageal contractions as they relate to pretreatment, HRM/EPT-defined subtypes.

Materials and Methods

Subjects

Fifty-one patients with achalasia (age, 19–82 y; 21 women) without previous pneumatic dilation or esophageal myotomy who had FLIP completed during endoscopy were included. Five patients had received previous botulinum toxin injections (at 3/3, 5/5, 5/4, 62/62, and 196/196 months before FLIP/HRM). Patients presented to the Esophageal Center of Northwestern for the evaluation of dysphagia, noncardiac chest pain, and/or regurgitation from November 2012 to June 2015. Achalasia was diagnosed and subclassified by HRM (4.2-mm outer diameter, solid-state assembly with 36 circumferential pressure sensors spaced 1-cm apart; Medtronic, Inc, Shoreview, MN) of 10 supine, 5-mL water swallows. By using Manoview analysis software version 3.0 (Medtronic), EPT was analyzed by measurement of the integrated relaxation pressure, distal latency, and esophageal body pressurization patterns.[3] All patients had a median integrated relaxation pressure greater than 15 mm Hg. Type I (classic) achalasia (n = 15) was defined by absent contractility in 100% of swallows. Type II achalasia (N = 26) was defined by panesophageal pressurization at an isobaric contour of 30 mm Hg in more than 20% of swallows. Type III (spastic) achalasia (N = 10) was defined by 20% or more premature swallows (ie, distal latency < 4.5 s).

Ten asymptomatic healthy volunteers (age, 20–49 y; 6 women) were included as a control group. These subjects have been described previously.[18,20] None of the subjects had a history of malignancy, gastrointestinal surgery, or endoscopic evidence of hiatal hernia, esophagitis, stricture, and/or mucosal changes suggestive of eosinophilic esophagitis. Control subjects did not undergo manometry as part of this study protocol. Informed consent was obtained from each subject.

The study protocol was approved by the Northwestern University Institutional Review Board.

Functional Lumen Imaging Probe System and Study Protocol

The FLIP assembly consisted of a 240-cm long, 3-mm outer diameter catheter with an infinitely compliant bag (up to a distension volume of 60 mL) mounted on the distal 18 cm of the catheter. The bag, tapered at both ends to assume a 16-cm long cylindric shape in the center that formed the impedance planimetry segment, housed 17 ring electrodes spaced 1-cm apart and a solid-state pressure transducer positioned at the distal end to provide simultaneous measurement of 16 channels of cross-sectional area (CSA) and intrabag pressure. The impedance planimetry segment had a minimum-to-maximum range of measureable CSA within the infinitely compliant range of 21–380 mm^2; assuming circular lumen cross-sections, this corresponded to a diameter of 5.2–22 mm. Pressure values greater than 380 mm^2 (22-mm diameter) could be measured, but mechanical properties of the bag would be engaged above this distension range. Measurements from the impedance planimetry electrode pairs and the pressure transducer were sampled at 10 Hz with the data acquisition system and transmitted to the recording unit.

Subjects underwent upper endoscopy in the left lateral decubitus position. Moderate sedation with 2–12 mg midazolam and 0–250 μg fentanyl was administered during the procedure. Propofol was used in addition to midazolam and fentanyl, with anesthesia assistance at the discretion of the endoscopist in 4 patients. The FLIP probe was placed transorally and positioned with the distal 1–3 impedance sensors beyond the EGJ as confirmed by demonstration of a narrowing in the impedance planimetry segment at a bag distension volume of 20–30 mL. The endoscope was withdrawn before initiation of the FLIP study protocol. The FLIP assembly position was adjusted by the endoscopist during the study to maintain placement relative to the EGJ as visualized on real-time output. Simultaneous CSAs and intrabag pressures were measured during 5-mL, step-wise distensions beginning with 5 mL and increasing to a target volume of 60 or 70 mL. Each step-wise distension volume was maintained for 5–20 seconds during a single-distension protocol for each patient; examples of the distension protocol can be observed in the volume plots of figures illustrating FLIP topography. The distension protocol changed during the course of the evaluation period, initially the limit was 60 mL and later the limit was 70 mL. The recording unit was set to stop infusing and show an alarm message if the intrabag pressure exceeded 60 mm Hg, which sometimes limited the extent of bag distension.

FLIP Data Analysis

Data including distension volume, intrabag pressure, and 16 channels of CSA measurements (via impedance planimetry) for the entire study for each subject were exported to MATLAB (The Math Works, Natick, MA) for analysis using a customized MATLAB program. This program applied a filter to minimize vascular and respiratory artifact, and then generated tracings of each channel's measured luminal diameter. Interpolation of each channel's diameter measurement was applied to generate color-coded topography plots with corresponding plots of volume distension and intrabag pressure by time (Figure 1 shows an example of a normal control). The program identified the EGJ midline by searching for the minimal CSA of the distal impedance planimetry channels. The EGJ-distensibility index (EGJ-DI) was calculated by measuring the narrowest EGJ CSA and intrabag pressure at each data sample (10 per second) obtained during the time course at distension volumes of 50 and 60 mL (corresponding to the 30- and 40-mL distension