ALIMENTARY TRACT

Esophageal Distensibility as a Measure of Disease Severity in Patients With Eosinophilic Esophagitis

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BACKGROUND & AIMS: **The aim of this study was to assess whether measurements of esophageal distensibility, made by high-resolution impedance planimetry, correlated with important clinical outcomes in patients with eosinophilic esophagitis.**

METHODS: **Seventy patients with eosinophilic esophagitis (50 men; age, 18–68 y) underwent endoscopy with esophageal biopsy collection and high-resolution impedance planimetry using the functional lumen-imaging probe. The patients were followed up prospectively for an average of 9.2 months (range, 3–14 mo), and the risk of food impaction, requirement for dilation, and symptom severity during the follow-up period was determined from medical records. Esophageal distensibility metrics and the severity of mucosal eosinophilia at baseline were compared between patients presenting with and without food impaction and those requiring or not requiring esophageal dilation. Logistic regression and stratification assessments were used to assess the predictive value of esophageal distensibility metrics in assessing risk of food impaction, the need for dilation, and continued symptoms.**

RESULTS: **Patients with prior food impactions had significantly lower distensibility plateau (DP) values than those with solid food dysphagia alone. In addition, patients sustaining food impaction and requiring esophageal dilation during the follow-up period had significantly lower DP values than those who did not. The severity of mucosal eosinophilia did not correlate with risk for food impaction, the requirement for dilation during follow-up evaluation, or DP values.**

CONCLUSIONS: **Reduced esophageal distensibility predicts risk for food impaction and the requirement for esophageal dilation in patients with eosinophilic esophagitis. The severity of mucosal eosinophilia was not predictive of these outcomes and had a poor correlation with esophageal distensibility.**

Keywords: Eosinophilic Esophagitis; High-Resolution Impedance Planimetry; Esophageal Distensibility; Functional Luminal-Imaging Probe; Dysphagia.

Eosinophilic esophagitis (EoE) is a disease of increasing prevalence[1] possibly related to a higher incidence of allergic diseases and to a greater awareness in specific patient populations.[2,3] Patients present with a spectrum of esophageal symptoms[4]; however, the dominant symptoms in adults are dysphagia, food impaction, and, less commonly, chest pain.[5] These symptoms are thought to result from the consequences of an allergic immune response that involves T-cell–mediated hypersensitivity and IgE-mediated pathways, leading to eosinophil activation with the consequence of tissue remodeling and fibrosis.[6]

The current clinical paradigm for diagnosing and assessing EoE is focused on endoscopic biopsies. Specifically, the greatest observed density of eosinophils per high-power field (hpf) is used as a diagnostic test: patients with a positive biopsy (≥15 eosinophils/hpf) should receive a trial proton pump inhibitor (PPI) and undergo a biopsy again to confirm the diagnosis of

Abbreviations used in this paper: CSA, cross-sectional area; DP, distensibility plateau; DS, distensibility slope; EGJ, esophagogastric junction; EoE, eosinophilic esophagitis; FLIP, functional luminal imaging probe; hpf, high-power field; PPI, proton pump inhibitor; PPI-R-EE, PPI-responsive esophageal eosinophilia.

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EoE (second eosinophil count, ≥15/hpf). Patients with a density of eosinophils less than 15/hpf after PPI therapy are categorized as PPI-responsive esophageal eosinophilia (PPI-R-EE). The density of eosinophils also is used as a clinical indicator of disease activity.[2] However, that approach largely ignores the dominant clinical and pathologic features of the disease, which are luminal stiffening and narrowing associated with esophageal wall thickening,[7] edema, fibrosis, and stricture. Although endoscopic features are used to assess disease activity,[8] the endoscopic assessment is hampered by poor reproducibility and an inability to measure abnormalities directly in esophageal wall biomechanics related to tissue remodeling. Recently, our group refined a modified high-resolution impedance planimetry technique to quantify the pressure-geometry relationship in the esophagus.[9] The functional lumen-imaging probe (FLIP) uses high-resolution impedance planimetry to render a 3-dimensional approximation of intraluminal esophageal anatomy during volumetric distention. Our initial results suggested that EoE patients had reduced esophageal distensibility compared with controls. However, we were unable to determine whether esophageal distensibility could inform clinical outcome and function as a biomarker of EoE disease activity.

Thus, the aim of this study was to assess whether esophageal distensibility metrics correlated with susceptibility to food impaction and/or the subsequent requirement for esophageal dilation during follow-up evaluation. In addition, we sought to compare esophageal distensibility with the severity of mucosal eosinophilia as an outcome measure by correlating each with symptom severity during follow-up clinical evaluation.

Methods

Subjects

Seventy-seven patients (55 men; age, 18–68 y), who presented to the Esophageal Center at Northwestern from July 2009 to May 2012 with food impaction, dysphagia, chest pain, or heartburn, and histology reporting 15 or more eosinophils/hpf (magnification, 0.196 mm^2),[10] were enrolled to assess the biomechanical properties of the esophageal wall.[9] After a trial of PPI therapy, a second endoscopy with repeated biopsies and high-resolution impedance planimetry using the FLIP device was performed to classify the patients as EoE (eosinophil count, ≥15/hpf) or PPI-R-EE (eosinophils, <15/hpf). Each patient was cared for by 1 of the 4 esophagologists after the FLIP protocol and was treated at that physician's discretion. Symptoms were assessed at the 12-month follow-up evaluation (a shorter follow-up period was used if patients required immediate intervention). None of the subjects had a history of gastrointestinal surgery or malignancy. A group of 10 normal controls underwent endoscopy to confirm a lack of endoscopic findings consistent with EoE and FLIP protocol for comparison. The study protocol was approved by the Northwestern University Institutional Review Board and informed consent was obtained from each subject.

Functional Luminal Imaging Probe System

The FLIP assembly[9,11,12] was built on a 240-cm–long catheter with a 3-mm outer diameter. An infinitely compliant bag (with a volume limit up to 50 mL) sealed to the distal 14 cm of the probe was created to assume a 10-cm–long cylindric shape between tapering ends. The minimal-to-maximal range of cross-sectional area (CSA) measurable was 10 to 491 mm^2. The 8-cm segment within the bag designed for impedance planimetry measurement comprised 16 ring electrodes spaced 5-mm apart. The assembly also contained a solid-state pressure transducer for determining intrabag pressure. Measurements were sampled at 10 Hz.

Study Protocol

Subjects underwent endoscopy with a 9.9-mm outer-diameter diagnostic gastroscope (Olympus GIF type H180J; Olympus Corporation, Tokyo, Japan), in the left lateral decubitus position to evaluate for EoE findings, esophagogastric junction (EGJ) location, and to help position the FLIP. Moderate sedation with 5 to 10 mg midazolam and 0 to 200 μg fentanyl was administered during the procedure. Still images taken during endoscopy were graded by a blinded investigator (J.C.) for major EoE structural features of the grading system proposed by Hirano et al.[8] Ring score was graded as follows: 0, none; 1, mild for subtle circumferential ridges; 2, moderate for distinct rings that do not impair passage of a standard diagnostic adult endoscope; or 3, severe for distinct rings that do not permit passage (of a diagnostic endoscope). Focal stricture score was graded as follows: 0, absent; or 1, present. Exudate score was graded as follows: 0, none; 1, mild for lesions involving less than 10% of the esophageal surface area; or 2, severe for lesions involving more than 10% of the esophageal surface area. Furrow score was graded as follows: 0, absent; or 1, present.

After endoscopy, the FLIP probe was placed transorally across the EGJ.[9] Volume distension was performed to localize the EGJ and then position the FLIP with the distal recording site 3 cm proximal to the EGJ. Esophageal CSAs were measured during 2-mL stepwise distensions beginning with 2 mL and increasing to a maximum of 40 mL (each step was recorded for

Table 1. Baseline Data Before Intervention

Patient characteristics	
Male, n (%)	50 (71)
Median age, *y* (range)	38 (18–68)
Presenting symptom, n (%)	
Food impaction	26 (37)
Dysphagia alone	37 (53)
Chest pain	5 (7)
Heartburn	2 (3)
Endoscopic findings,[a] n (%), may be multiple	
Rings	66 (94)
Grade 1: mild	40 (57)
Grade 2: moderate	17 (24)
Grade 3: severe	9 (13)
Focal stricture (present)	34 (49)
Exudates	35 (50)
Grade 1: mild	31 (40)
Grade 2: severe	4 (6)
Furrows	56 (80)
Grade 1: mild	55 (79)
Grade 2: severe	1 (1)
Primary treatment, n (%), may be multiple	
Discontinued PPI	10 (14)
Continued PPI therapy	54 (78)
Swallowed topical steroids	7 (10)
Diet	4 (6)

[a]Endoscopic features were graded according to Hirano et al.[8]