Title

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Esophageal compliance quantifies epithelial remodeling in pediatric patients with eosinophilic esophagitis

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Abstract

Background: The management of eosinophilic esophagitis (EoE) relies on the severity of esophageal eosinophilia, yet there is poor evidence of its prediction of esophageal fibrotic remodeling and subsequent complications such as dysphagia, food impactions, or strictures. Functional Luminal Impedance (FLIP) has had limited use in pediatric patients to evaluate esophageal tissue mechanics. We aimed to standardize the FLIP technique and to measure esophageal compliance in children with EoE in comparison to controls.

Methods: Subjects were enrolled into a prospective observational study and had FLIP performed at the time of endoscopy. We calculated esophageal distensibility and compliance for the total and segmental esophagus independently (i.e., proximal, middle and distal esophageal segments). We evaluated esophageal biopsies for eosinophilia and epithelial remodeling, calculated endoscopy scores, and documented patient symptoms.

Results: We enrolled 11 EoE and 12 controls subjects, aged 5–18 years old. While EoE subjects had lower esophageal compliance (p=0.004) than controls, the difference in distensibility did not reach significance (p=0.151). Epithelial remodeling severity was more strongly correlated with compliance than with distensibility. Epithelial remodeling scores ≥2 had a significant association with lower compliance both segmentally and in the entire esophagus (p=0.029), but not with

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distensibility. Compliance measures were more sensitive in detecting subjects with remodeling score ≥2 than distensibility (79% versus 64%).

Conclusion: Compliance is a more sensitive measure of esophageal epithelial remodeling in children compared to distensibility, and a more appropriate measure of esophageal tissue mechanics. Standardized placement of the FLIP catheter is important to accurately assess esophageal compliance.

Introduction

Eosinophilic esophagitis (EoE) is an antigen driven T_H2 inflammatory disorder, whereby esophageal eosinophilic, mastocytic, and T cell inflammation results from repeated exposure to food and/or aeroallergens. This chronic inflammation can lead to structural remodeling, ultimately resulting in esophageal strictures, food impactions, symptoms reflective of esophageal dysfunction, and dysmotility.(1)

The current paradigm for diagnosing and grading response to therapeutic interventions depends on quantifying eosinophilic density in esophageal biopsies.(2, 3) This method of monitoring for clinical response and resolution of inflammation has multiple limitations. While biopsies assess inflammation, they cannot routinely gauge esophageal fibrosis and do not monitor functional esophageal outputs. Remodeling changes, including lamina propria fibrosis, increased vascularity, and expansion of the muscularis propria, can be difficult to obtain on superficial biopsy due to a paucity of deep tissue layers.(4) In addition, symptoms in pediatrics do not reflect disease course or complications(5) and it is unclear why children sometimes remain symptomatic despite inflammatory resolution. Since treatment non-uniformly reverses structural remodeling,(6–8) there is a clinical concern that unappreciated structural remodeling may be causing symptoms. As such, the use of a supplemental tool to assess remodeling changes would be useful in pediatric EoE.

The Functional Luminal Imaging Probe (FLIP) uses impedance planimetry to investigate pressure and cross-sectional area relationships during serial volumetric distensions, thereby measuring both distensibility and compliance. FLIP can thus be used to assess esophageal tissue mechanics, which we hypothesize will correlate with structural remodeling on a molecular level. While adult and pediatric studies have reported decreased distensibility in EoE subjects compared to asymptomatic controls,(9–12) compliance has not been evaluated in children and prior studies have not correlated such measures with the location of the esophageal biopsies. In addition, if FLIP were to be utilized more routinely in children, a uniform protocol for positioning the FLIP probe would be necessary. In this study, we aim to investigate whether esophageal compliance or distensibility is a more sensitive measure in detecting epithelial remodeling on a segmental and global level in children. We hypothesized that compliance would be a stronger indicator of remodeling than distensibility.

Methods

Study Design and Patient Selection

Subjects aged 5–18 years were recruited from the University of California San Diego and Rady Children's Hospital–San Diego Pediatric Gastroenterology, Eosinophilic Esophagitis,

and Motility clinics into a prospective observational study based on a history of known or possible EoE, symptoms of dysphagia, food impaction, or food avoidance along with a plan for upper endoscopy and FLIP as part of routine clinical care. Subjects were assigned to the control group if the endoscopy with biopsy was not consistent with EoE. In controls with persistent dysphagia, an upper GI and esophageal manometry were performed to rule out structural abnormality or primarily motility disorder. They were ultimately diagnosed with one of the following diagnoses: GERD, functional dysphagia, supragastric belching, or gastritis. Subjects were diagnosed with EoE based on finding > 15 eosinophils/hpf on hematoxylin and eosin staining at 400x light microscopy after at least two months of high dose proton pump inhibitor (PPI) treatment. Subjects were excluded if they had PPI Responsive Esophageal Eosinophilia (PPI-REE), defined as resolution of esophageal eosinophilia when on PPI, or other causes of esophageal eosinophilia such as Crohn's Disease.

Power analysis revealed a sample size of 22 subjects to detect a 10% difference in esophageal diameter between patients with EoE and controls. The following assumptions were made in the calculation: 1) 95% of healthy children have normally distributed esophageal diameters between 20–25mm; 2) There is a medium amount of variation of cross-sectional area (CSA) throughout the esophagus between subjects themselves; 3) There is a 10% margin of error in calculating esophageal CSA when considering changes with respiration. The University of California San Diego and Rady Children's Hospital–San Diego Institutional Review Boards approved the study protocol. The following information was recorded: history of atopy, food impaction, family history, and results of upper GI, esophageal manometry, and endoscopy.

Endoscopic Functional Luminal Imaging Probe (FLIP) System and Protocol

Subjects underwent esophagogastroduodenoscopy (EGD)under general anesthesia at the discretion of the pediatric anesthesiologist. The position of the upper and lower esophageal sphincters were noted by the endoscopist during EGD, and FLIP was performed prior to obtaining esophageal biopsies. FLIP assembly catheter size – 16cm compliant to 60mL or 8cm compliant to 40mL – was chosen based on the subject's height (See Text, Supplemental Digital Content 1). The FLIP probe was placed transorally into the esophagus, advanced to the presumed location of the gastroesophageal junction (GEJ), and balloon inflated to 20mL to verify the GEJ position. The balloon was then deflated, and the position of the catheter was adjusted to center it between the upper esophageal sphincter (UES) and GEJ. Simultaneous esophageal CSAs and intra-bag pressures were measured in 5mL incremental bag distensions starting at 20mL. Each distention volume was maintained for 5–15 seconds to allow for equilibration. A maximum pressure of 60mmHg was tolerated. If this pressure wasn't reached, a maximum of 40mL or 60mL was instilled for the 8cm and 16 cm catheter, respectively.

Data Analysis

Data were analyzed using custom code developed in Python v3.6.3 using Jupyter Notebook with the following modules: Numpy v1.13.3, Scipy v0.19.1, Pandas v0.20.3, Matplotlib v2.1.0 and Seaborn v0.8. Distension volumes, intra-balloon pressures, and 16 channels of

diameter measurements for the entire study for each subject were exported to Python. The locations of the GEJ and UES were entered manually. As previously described(11), a median filter with a five second window size was applied to measured diameters and intra-bag pressures to minimize vascular and respiratory artifact. As some patients have esophageal contractions during the study, the nadir pressure and maximum diameter values were identified for each distention volume to reflect the relaxed state of the esophagus.(11) The program removed data that included or crossed any sphincters, and no data was entered for the resulting esophageal segment that did not get measured.

We defined distensibility as the minimal cross sectional area at maximal intrabag pressure.(12) In other studies, this value is called the distensibility plateau.(9, 11) Compliance was defined as the slope of the best-fit line through the pressure-volume curve. The volume was expressed as percentage of maximal infused volume (%volume) to account for the use of different catheter sizes.

Segmental data

When measuring distensibility and compliance for segmental data, the catheter was not moved or repositioned, but read by segment. Distensibility of the proximal, middle, and distal esophagus was represented by the narrowest CSA at each corresponding segment at maximal intrabag pressure. The Python program was used to calculate compliance. For segmental compliance, the volume is expressed as %volume infused due to use of different catheter sizes and differing maximal volumes per segment. This is under the assumption that esophageal pressure remains equal at each segment.

Histologic and endoscopic assessment

Biopsies from the proximal, middle, and distal esophagus were examined by hematoxylin and eosin stain, by a single pathologist blinded to the therapy. The numbers of epithelial eosinophils, lamina propria (LP) fibrosis, and epithelial remodeling score that includes basal zone hyperplasia severity, presence or absence of dilated intercellular spaces, and desquamation, were quantified by using our previously published pathology scoring tool.(6, 13) Each endoscopy was assigned a score measuring EoE severity based on Endoscopic Reference Score (EREFS).(14)

Symptoms

The Pediatric Eosinophilic Esophagitis Symptom Score (PEESS™ v2.0) was used to collect patient symptoms at the time of FLIP.(15)

Statistical Analysis

Significance between variables by group was determined by a Mann Whitney U-test for continuous variables and Fisher’s exact test for categorical variables. Relationships between continuous variables were assessed with Spearman correlation coefficient, which was repeated for the entire data set and within each group – EoE and control. This was repeated on a segmental level, with segmental compliance and distensibility correlated to histology scores for each respective level of the esophagus. Receiver operating characteristic (ROC) analysis was performed in order to measure the sensitivity and specificity of compliance and

distensibility in detecting an abnormal epithelial remodeling score of two or more. A cutoff of two was used, as epithelial remodeling scores of ≥ 2 are seen in patients with active EoE (6). In this analysis, the proximal, middle, and distal segments from the same patient were treated as independent.

Results

Baseline Clinical Data

Twenty-three subjects were evaluated: 12 controls and 11 EoE. There was no significant difference in the age or gender between groups (Table 1). Approximately half of the EoE group had an atopic diathesis of asthma, allergic rhinitis, eczema, or food allergy. None of the subjects had a history of food impaction. Thirteen subjects, six controls and seven EoE patients, had an upper GI study. All upper GI studies were read as normal. One EoE patient had easy passage of the GIF H190 upper endoscope, with an external diameter of 9.2mm, but with subsequent FLIP, was noted to have an area of decreased esophageal expansion. The patient was re-evaluated by EGD and documented to have a subtle stricture. We did not exclude this patient in order to study patients with a broad disease spectrum. Nevertheless, analyses done with and without this patient yielded the same conclusions.

Symptom duration was significantly longer in the EoE group (p=0.016), though the type of symptoms experienced by the two groups was not significantly different, likely due to the clinical entry criteria required for performing FLIP (Table 1). The majority of control subjects were treatment naïve while the majority of EoE subjects remained symptomatic despite EoE-directed therapy. Of the 11 patients with EoE, seven had active EoE. Three subjects were newly diagnosed with EoE upon recruitment, four subjects had been diagnosed for 1–4 years, and four subjects had been diagnosed for 5–9 years. Of the three newly diagnosed EoE, two were off therapy for the study and later had a scope after two months of PPI therapy with ≥ 15 eos/hpf; the other had been on more than two months of PPI at time of study, but previously had a scope off therapy with biopsies showing ≥ 15 eos/hpf. Table, Supplemental Digital Content 2 shows further characteristics of the EoE groups.

Eosinophilic density was significantly higher in EoE compared to controls (86 versus 1, p<0.001). Of the 12 controls, 11 had 1 eos/hpf and one had 8 eos/hpf; the latter was not on any medications. In addition, the maximum epithelial remodeling score in the EoE group was significantly higher than in controls (2.27 versus 0.08, p=0.001). Among subjects with lamina propria available on biopsy (64% of EoE, 33% of controls) EoE subjects had significantly higher fibrosis scores (2.71 versus 0.5, p=0.015).

Esophageal Distensibility

Distensibility was defined as the minimal CSA of the esophagus at maximal intrabag pressure. It was not significantly different in the EoE group compared to the control group (168 [range 85–270] cm^2 versus 196 [range 120–290] cm^2, p=0.151; Table 1) nor was it significantly different in patients with active versus inactive EoE (153 [range 85–236] cm^2 versus 195 [range 141–270] cm^2, p=0.164, Table, Supplemental Digital Content 2). We evaluated the association between distensibility and remodeling, eosinophilic inflammation,

and symptoms (Table, Supplemental Digital Content 3). There was a significant inverse correlation between the distensibility and maximum epithelial remodeling score (r=−0.46, p=0.026). There was a trend toward significance between distensibility and eosinophilic density (r=−0.39,p=0.065)

An analysis by esophageal segment demonstrated a significant inverse correlation between distensibility and epithelial remodeling score in middle and distal segments (middle r=−0.62, p=0.002; distal r=−0.63, p=0.001) and between distensibility and eosinophilic density in the middle segment (middle r=−0.66, p=<0.001) (Table 2). The inverse correlation signifies that lower distensibility correlates with increased epithelial remodeling and increased eosinophilic inflammation. In contrast, there were no significant correlations between distensibility and symptoms including total score, subdomain score, or duration.

Esophageal Compliance

Compliance curves were significantly different between EoE and control subjects (p=0.004; Figure 1). Compliance values were also significantly different between the two groups (Table 1). There was a significant inverse correlation between compliance and epithelial remodeling score (r=−0.67, p=0.001), eosinophilic density (r=−0.57, p=0.004), and lamina propria fibrosis (r=−0.81, p=0.003) over the total esophagus (Table, Supplemental Digital Content 4). Analysis by segments revealed a significant inverse correlation between compliance and epithelial remodeling score across the proximal (r=−0.44, p=0.034) and middle segments (r=−0.73, p<0.001) (Table 2). There also was a significant inverse correlation between compliance and eosinophilic density in the middle segment (r=−0.68, p=<0.001). The inverse correlations signify that decreased compliance is associated with increased epithelial remodeling and eosinophilic inflammation. Like distensibility, there were no significant correlations between compliance and symptom scores, but there was a significant inverse correlation with symptom duration (r=−0.52, p=0.012).

We evaluated compliance and distensibility, by segment, in control patients to determine if there were any regional differences at baseline. While there was no difference in compliance between segments, there was significantly decreased distensibility in the proximal compared to middle (p=0.009) and proximal compared to distal (p<0.001) segments (Table, Supplemental Digital Content 5).

A linear mixed model was used to assess compliance in subjects with high versus low epithelial remodeling scores and fibrosis scores. The cutoff of two was chosen to represent remodeling that could not be attributed to gastroesophageal reflux alone.(6) When all segments were included, those with an epithelial remodeling scores ≥2 had a significantly lower compliance, with a slope difference of 0.67 (p=0.029). This was also true when each segment was evaluated separately. Those with fibrosis scores ≥2 also had a significantly lower compliance, with a slope difference of 1.17 (p=0.013). A similar analysis done for distensibility showed less clinical significance (p=0.097 for epithelial remodeling ≥2 and p=0.046 for fibrosis ≥2).

Sensitivity and specificity of esophageal distensibility versus compliance in detecting histologic remodeling

Plots of the area under the ROC (AUROC) curve for epithelial remodeling score ≥2 and compliance or distensibility as the diagnostic variable showed that compliance is a better predictor of histologic remodeling than distensibility (Figure 2), albeit not significantly (p=0.191). The AUROC for compliance as a predictor of epithelial remodeling score ≥2 was 0.83 (95% CI: 0.71 to 0.94), and that for distensibility was 0.74 (95% CI: 0.60 to 0.88). The values that maximized sensitivity and specificity for compliance and distensibility were 0.65 %mL/mmHg and 184mm^2, respectively. At these values, compliance had a higher sensitivity (79% versus 64%) and the same specificity (77% versus 77%) compared to distensibility at predicting abnormal epithelial remodeling scores.

The Relationship of endoscopic scoring to Compliance and Distensibility

Both distensibility and compliance inversely correlated with edema (r=−0.43, p=0.042; r=−0.45, p=0.033), furrows (r=−0.42, p=0.044, r=−0.73, p<0.001), and the total EREFS score (r=−0.51, p=0.013, r=−0.68, p<0.001) (Table, Supplemental Digital Content 3 and Table, Supplemental Digital Content 4).

Discussion

The application of FLIP to EoE is a new technique that is increasingly being used to measure esophageal tissue mechanics. As such, FLIP may provide the first standardized functional parameter for a disorder in which the current primary management outcome is histology. In this paper, we present a number of novel findings when applying FLIP to pediatric subjects and specifically demonstrate the utility of esophageal compliance in analyzing remodeling in pediatric EoE.

In order to compare subject data across studies, it is imperative to have a consistent protocol for FLIP catheter placement. While some studies have performed the procedure with the FLIP probe positioned with the distal two sensors below the GEJ with the purpose of ensuring the catheter stays in place,(11, 12, 16) others have positioned the distal tip above the GEJ.(9, 10, 17) In our study, we purposely chose a catheter size (e.g., 8cm versus 16cm) to allow positioning of the FLIP probe centered between the UES and the GEJ. This technique offered a number of advantages: 1) accurate representation of isolated esophageal pressures, independent from sphincters; 2) evaluation of segmental portions of the esophagus; and 3) ability to procure biopsies at the site of catheter placement.

Unlike the prior pediatric study which showed that esophageal distensibility was decreased in EoE subjects compared to controls,(12) our data showed a significant difference in compliance but not distensibility between the two groups. There are a number of possible explanations for this difference. First, our patient population was smaller, and it is possible that larger numbers are needed to see statistical differences. Second, our population was distinct from that of Menard-Katcher et al(12) in that their control children had significantly larger diameters than ours (17.2±2.6 mm versus 15.2±1.8 mm), though our EoE diameters were similar (15.0±2.7 mm versus 14.5±2.3 mm). For this reason, we saw smaller

differences in the intergroup distensibility. Lastly, we compared segmental distensibility within the control group to demonstrate that distensibility was significantly lower in the proximal esophagus compared to middle and distal segments. This was not observed with compliance. This difference in proximal distensibility suggests that using the narrowest point of the esophagus to reflect structural changes in the esophagus as a whole may be misleading, especially if areas of physiologic narrowing, such as the aortic arch, influence it. This is further reflected in the lack of correlation between proximal esophagus distensibility and esophageal remodeling, whereas both the middle and distal segments had significant inverse correlation between distensibility and epithelial remodeling. The differences in the conclusions between our results and those of Menard-Katcher underscore the importance of standardizing the methodology and interpretation of FLIP in children with EoE.

In contrast to our distensibility results, our compliance data agrees with Kwiatek *et al.*, who demonstrated that the compliance curves differ between adult EoE and control patients.(9) Prior pediatric studies have not analyzed compliance. Compliance of the esophagus as a whole correlated significantly with epithelial remodeling and lamina propria fibrosis, as well as symptom duration. When analyzing segmental data, we found stronger correlations between compliance and both epithelial remodeling as well as eosinophilic density in the proximal and middle esophagus. These findings highlight the importance of evaluating compliance of esophageal segments and suggest that functional alterations in the EoE esophagus may be better gauged in the proximal and middle esophagus.

While the majority of studies published on FLIP have focused on esophageal distensibility as their measure of esophageal mechanics, we show that compliance may be a better measure of esophageal remodeling, at least in children. Unlike distensibility, compliance was significantly lower in subjects with epithelial remodeling scores that were ≥2 versus those that were <2. This cutoff was chosen since scores greater than two are unlikely to be a result of GERD alone. In addition, AUROC curves showed that compliance was a superior predictor of abnormal epithelial remodeling scores compared to distensibility, though this did not achieve statistical significance.

The fact that esophageal compliance is a more sensitive measure for the histologic features of epithelial inflammation and remodeling is likely due to the fact that compliance measurements take the entire esophagus into account as opposed to distensibility, which focuses on the narrowest point in the esophagus. In cases where the esophagus is rigid but not narrowed, the compliance will likely be a more sensitive gauge for assessing early functional alterations. This is particularly salient in young children in whom changes in esophageal biomechanics occur prior to the onset of frank esophageal stenosis. Indeed, if one goal of EoE-directed therapy is to alter the natural history to strictures, it is important to understand if therapy improves esophageal tissue biomechanics in children. Further, as discussed above, relying on esophageal diameter can lead to pitfalls in interpreting physiologic variability as narrowing.

Pediatric data, including ours, differs from that of adults; while pediatric subjects exhibit correlation between esophageal eosinophilia and both decreased distensibility(12) and compliance, adult data show no association between esophageal eosinophilia, decreased

distensibility,(9) and food impaction risk.(10) In addition, we found that endoscopic findings of furrows and the total EREFS score correlated significantly with decreased compliance and distensibility, edema correlated with compliance, and exudates correlated with distensibility. While rings and strictures are thought to represent a fibrotic phenotype, in children (12, 18) furrows can correlate with lamina propria fibrosis.(13) It is likely that pediatric patients have a mixed inflammatory and structural remodeling picture, and those that have long standing inflammation can lead to inflammatory burn out along with continued and irreversible remodeling. Techniques such as FLIP will be helpful in assessing the differences in esophageal function between children with inflammatory-fibrotic mixed disease and purely inflammatory disease. This information could be pivotal when deciding on the mode, duration, and nature of the therapies used in pediatric subjects.

Our study has a number of strengths, including the analysis of esophageal compliance and the method in which we performed the FLIP procedure. In addition, we used robust criteria for assigning the EoE population, where all but one had panesophageal inflammation after a PPI trial. Though patients were of different ages, there was no difference in age between groups. A limitation to our study is that the EoE subjects were on different medications and at different durations of diagnosis. Our study was not designed to detect a relationship between disease duration, therapy type, distensibility, and compliance. A larger prospective study is necessary to evaluate the effects of therapy on remodeling and how it correlates with FLIP results. In this vain, it is important to design longitudinal studies that will minimize the inter-patient heterogeneity. We would further suggest that such studies be designed to assess improvements in esophageal compliance as the primary outcome using a standardized approach for catheter placement. Further use of FLIP in pediatric EoE will provide novel and clinically important insights for the management of this chronic disease.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Conflict of Interest and Sources of Funding

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Study Highlights

WHAT IS KNOWN

- Chronic inflammation from eosinophilic esophagitis (EoE) can result in esophageal strictures and dysmotility.
- Studies suggest that esophageal tissue mechanics correlate with underlying remodeling changes.
- The optimal approach to measure and evaluate esophageal tissue mechanics has not been established.

WHAT IS NEW

- A standardized protocol to perform Functional Luminal Impedance Planimetry (FLIP) is suggested.
- Esophageal compliance is a superior measure of epithelial remodeling in pediatric EoE subjects compared to distensibility.
- Using compliance as a measure for tissue remodeling is suggested.

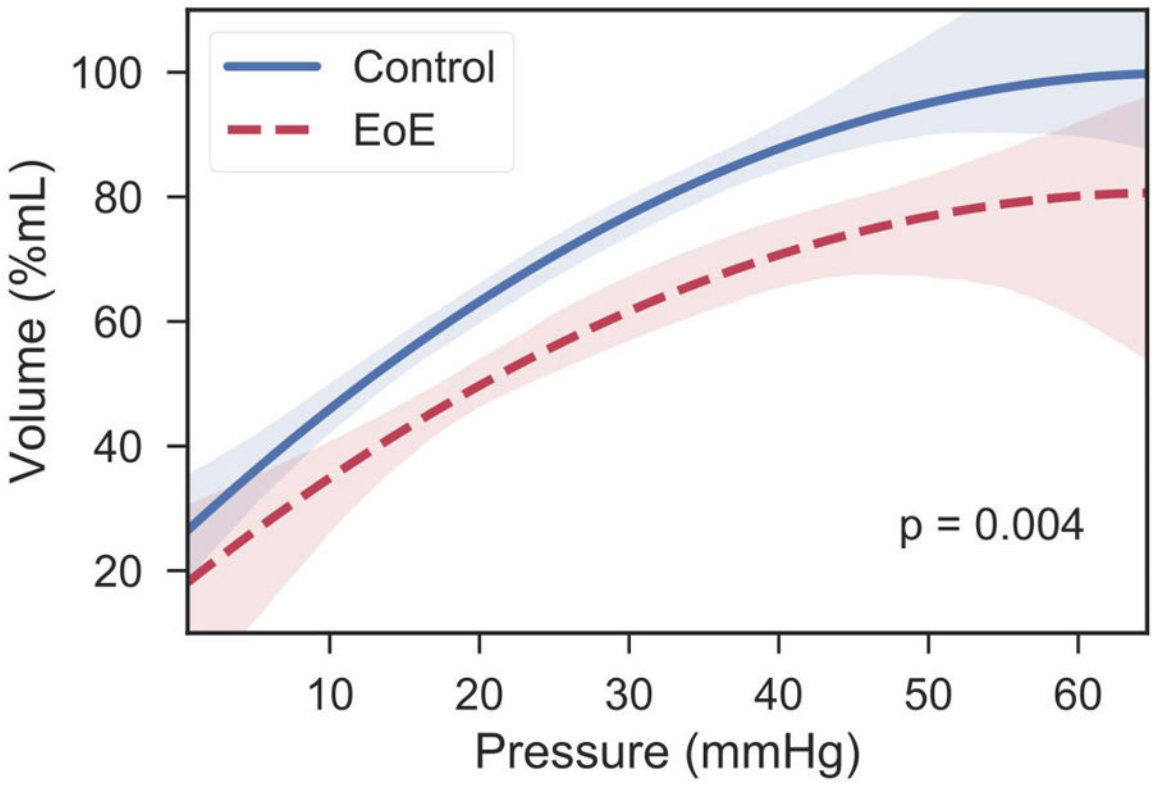

Figure 1.

Comparison of the esophageal compliance curves for EoE versus control groups, represented by best polynomial fit and with 95% confidence interval of the curves fitting the data. There is a significant difference in the pressure trajectories by group, with EoE subjects increasing pressure faster per unit increase in volume as compared to control subjects.

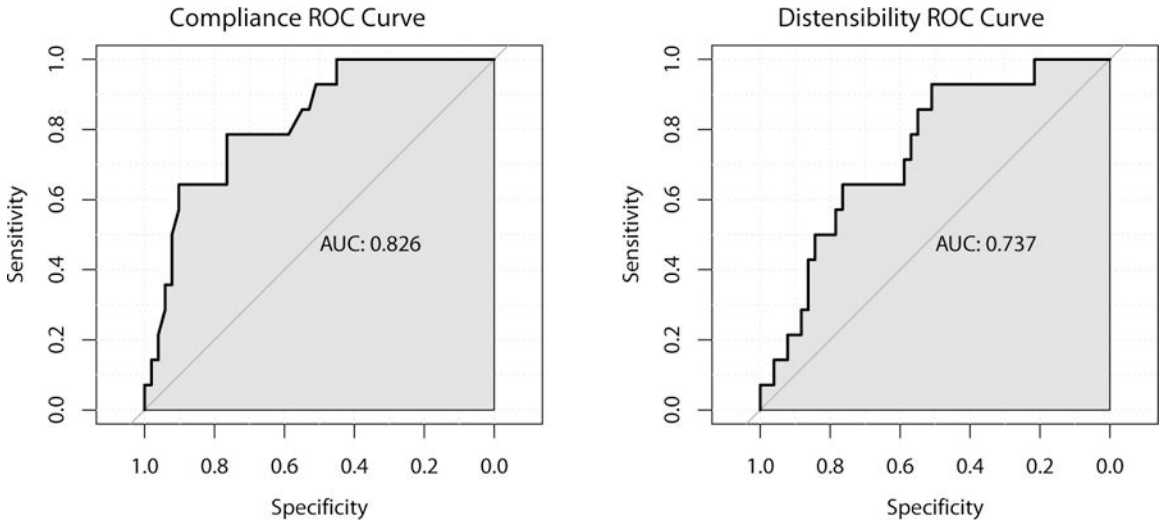

Figure 2.

Receiver Operator Characteristic (ROC) curves for epithelial remodeling score≥2 with compliance and distensibility as diagnostic variables. The Area Under ROC (AUROC) for compliance as a predictor of epithelial remodeling score ≥2 was higher than that for distensibility, though it did not reach significance, p=0.191.

Table 1.

Clinical Characteristics

	Control (n=12)	EoE (n=11)	p value
Subject Demographics			
Male	4 (33%)	8 (73%)	0.100
Age-years, mean (range)	10.4 (5–15)	12.8 (7–18)	0.130
Atopy			
Asthma	1 (8.3%)	6 (55%)	**0.027**
Eczema	3 (25%)	2 (18.2%)	1.000
Seasonal Allergies	6 (50%)	7 (63.6%)	0.680
Food Allergies	2 (16.7%)	5 (45.5%)	0.193
Positive Allergy Serum Screen	0 (0%)	4 (40%)	**0.029**
Family atopy history	8 (66.7%)	7 (63.6%)	1.000
UGI series			
Negative	6 (50%)	7 (63.6%)	0.680
Positive	0 (0%)	0 (0%)	n/a
Primary treatment, n (%)			
PPI monotherapy	2 (16.7%)	2 (18.2%)	0.923
Topical steroid + PPI	0 (0%)	5 (45.5%)	**0.006**
Diet + PPI	0 (0%)	1 (9.1%)	0.307
Diet alone	0 (0%)	1 (9.1%)	0.307
None	10 (83.3%)	2 (18.2%)	**<0.001**
Endoscopic Features, n (%)			
Edema/Decreased vascular markings	0 (0%)	5 (45.5%)	**0.006**
Rings/Trachealization	0 (0%)	0 (0%)	n/a
Exudates/Plaques	0 (0%)	3 (27.3%)	0.056
Furrows	0 (0%)	7 (63.6%)	**<0.001**
Strictures	0 (0%)	1 (9.1%)	0.307
Histology, mean (range)			
Maximum epithelial remodeling score	0.08 (0–1)	2.27 (0–5)	**0.001**
LP fibrosis *	0.5 (0–1)	2.71 (1–3)	**0.015**
Maximum eos/hpf in an esophageal biopsy	1.00 (0–8)	86.09 (0–165)	**<0.001**
Distensibility (mm^2), mean (range)	196 (120–290)	168 (85–270)	0.151
Compliance (%volume/mmHg), mean (range)	2.27 (0.93–4.88)	1.49 (0.39–6.39)	**0.004**
Symptoms, mean (range)			
Symptoms Duration-years	1.4 (0–6)	4.1 (1–9)	**0.016**
EoE Duration-years	n/a	2.9 (0–9)	n/a
Total symptoms score	32.7 (1.25–63.75)	40.70 (5–60)	0.423
Dysphagia symptom score	39.06 (3.13–84.38)	38.92 (0–68.75)	1.00

	Control (n=12)	EoE (n=11)	p value
Reflux symptoms score	27.60 (0–56.25)	28.98 (0–62.5)	0.925
Nausea symptom score	23.44 (0–62.5)	28.41 (0–68.75)	0.686
Pain symptom score	39.06 (0–68.75)	38.07 (0–75)	0.877

EoE, eosinophilic esophagitis; PPI, proton pump inhibitor; LP, lamina propria; eos/hpf, eosinophils per high power field

* LP was available in 7 EoE patients and 4 control patients

Table 2.

Correlation of Esophageal Distensibility and Compliance with Histologic Parameters, by segment

	Distensibility	p value	Compliance	p value
Max Epithelial remodeling score				
Proximal Esophagus	−0.23	0.304	−0.44	**0.034**
Middle Esophagus	−0.62	**0.002**	−0.73	**<0.001**
Distal Esophagus	−0.63	**0.001**	−0.20	0.371
Max Esophageal eosinophilia				
Proximal Esophagus	−0.24	0.264	−0.40	0.057
Middle Esophagus	−0.66	**<0.001**	−0.78	**<0.001**
Distal Esophagus	−0.35	0.103	−0.17	0.443

Max, Maximum