

## ORIGINAL RESEARCH—CLINICAL

## High-Resolution Esophageal Manometric Features in Eosinophilic Esophagitis Patients: A Retrospective Study

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**BACKGROUND AND AIMS:** Eosinophilic esophagitis (EoE) is an immune-mediated esophageal disease characterized by symptoms related to esophageal dysfunction and eosinophil-predominant inflammation. The aims of our study included (1) to assess esophageal motility patterns of EoE by topographic analysis of high-resolution manometry (HRM) and (2) to establish a relationship between symptoms of EoE and motility abnormalities seen on HRM. **METHODS:** A retrospective study in which all adult patients over 18 years of age with EoE diagnosed by endoscopy and histology and who underwent HRM were included in the study during the study period. Motility patterns in patients with EoE under HRM were analyzed. Data were presented as frequencies and percentages with inference by Pearson's chi-square test or Fisher's exact test. **RESULTS:** Seven hundred patients diagnosed with EoE were noted, and of these, 38 patients had undergone esophageal HRM. Fifty-eight percent of these patients were noted to have an esophageal motility abnormality on HRM. Thirty-seven percent of the patients showed absent peristalsis with pan-esophageal pressurization but normal integrate relaxation pressure; 21% of the patients showed peristaltic dysfunction; and 42% of the patients had a normal HRM. Seventy-one percent of the patients with pan-esophageal pressurization presented with food impaction requiring endoscopy for disimpaction and esophageal dilation ( $P = .015$ ). **CONCLUSION:** The most common abnormality noted was aperistalsis with pan-esophageal pressurization. This abnormality correlated with the clinical presentation of bolus impaction requiring an endoscopic intervention ( $P = .015$ ).

**Keywords:** High-Resolution Manometry; Eosinophilic Esophagitis; Dysphagia; Pan-Esophageal Pressurization

## Introduction

Eosinophilic esophagitis (EoE) is a chronic inflammatory esophageal disease with esophageal dysfunction secondary to eosinophil-predominant inflammation.<sup>1,2</sup> The disease is defined by the existence of esophageal dysfunction along with at least  $\geq 15$  eosinophils per high-power field on esophageal biopsy in the absence of other causes of eosinophilia like achalasia or primary gastroesophageal reflux disease.

It is mostly reported in males with 3:1 male-to-female predominance. Patients generally present with dysphagia and food impaction. Esophageal findings of mucosal edema, circular rings, and tube-like esophagus with or without strictures are mostly responsible for the symptom presentation of dysphagia and food impaction. However, there could be some esophageal motor pressure changes that can contribute to the symptoms either independently or in conjunction with endoscopic mucosal findings of the esophagus.

High-resolution esophageal manometry (HRM) is being increasingly utilized in the management of patients presenting with gastroesophageal reflux disease (GERD) and dysphagia. It has become the method of choice in the evaluation of esophageal motility and has replaced conventional manometry, due to its technical advantages and better reproducibility.<sup>3,4</sup> Only a few studies have shown esophageal motility abnormalities in EoE using HRM. Hejazi et al<sup>5</sup> found 50% of EoE patients to have major smooth muscle impairment on HRM. Nennstiel et al<sup>6</sup> studied 20 EoE patients and found abnormal esophageal motility in 35% of patients on HRM. Martín Martín et al<sup>7</sup> found that pan-esophageal pressurization was the most common finding among 21 patients.

We aim to study and categorize motor disorders of the esophagus in EoE utilizing HRM and analyze the relationship between motility abnormalities and symptom presentation in EoE patients.

## Methods

A retrospective analysis of adult patients over 18 years of age diagnosed with EoE and evaluated with high-resolution

**Abbreviations used in this paper:** EGJ, esophagogastric junction; EoE, eosinophilic esophagitis; GERD, gastroesophageal reflux disease; HRM, high-resolution manometry; IRP, integrate relaxation pressure; LES, lower esophageal sphincter.

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manometry was conducted at the Albany Medical Center, Albany, New York, between January 2010 and January 2021. This study was approved by the institutional review board at our institution and registered under the protocol number 6177. Given the retrospective nature of the study, requirements for informed written consent were waived. Patients with a confirmed clinicopathologic diagnosis of EoE who were evaluated with HRM were included in the study.

Out of 700 patients with a confirmed histologic diagnosis of EoE per the American Gastroenterological Association definition,<sup>8</sup> 38 patients underwent HRM for further evaluation of their symptoms.

Patients with EoE under the age of 18 years and those with EoE who did not undergo HRM were excluded.

A total of 700 patients with a diagnosis of EoE during the study period were reviewed in our electronic medical record manually. A chart review of all these 700 patients showed that 38 patients underwent HRM.

Patient data collected included demographics; comorbidities; laboratory parameters; EoE treatment received, including proton pump inhibitors and corticosteroids; endoscopic findings; and HRM findings and parameters.

An analysis was performed to determine the motility patterns in EoE patients on HRM, the most common motility abnormality, and the association between the clinical symptoms and the HRM findings in EoE patients.

### Statistical Analysis

Categorical data were presented as frequencies and percentages with inference by Pearson's chi-square test or Fisher's exact test if the expected value in any cell was less than 5.

## Results

### Demographic, Clinical, and Endoscopic Characteristics of Study Patients

Between January 2010 and January 2020, 700 patients who had undergone endoscopic and histologic diagnosis of EoE were identified. Of these patients, 38 underwent esophageal HRM. The study population had a mean age of  $29 \pm 11$  years and consisted of 25 (66%) male patients and 13 (34%) female patients. Among these patients, 28 (74%) were white, 3 (8%) were Hispanic, 6 (16%) were black or African American, and 1 (2%) was Asian. Of the 38 EoE patients with HRM analysis, 9 (24%) had a pre-existing diagnosis of asthma, and 7 (18%) had a pre-existing diagnosis of allergic rhinitis. Additionally, of these 38 cases, 37 (97%) reported clinical symptoms of dysphagia, 21 (55%) had bolus impaction, 12 (32%) had heartburn, and 11 (29%) had GERD (Table 1).

Endoscopic findings revealed furrows in 11 patients, rings in 4 patients, both furrows and rings in 12 patients, white exudate in 4 patients, and stricture in 8 patients (Table 1).

### HRM Patterns in Study Patients

The mean resting pressure of the lower esophageal sphincter (LES) was measured at  $17 \pm 7$  mmHg; the LES

**Table 1.** Demographic, Clinical, and Endoscopic Characteristics of Patients With Eosinophilic Esophagitis (N = 38)

Demographics	
Age (y), mean (SD)	29 (11)
Male gender, N (%)	25 (66)
White race, N (%)	28 (74)
Allergic conditions	
Asthma, N (%)	9 (24)
Allergic rhinitis, N (%)	7 (18)
Clinical symptoms	
Dysphagia, N (%)	37 (97)
Bolus impaction, N (%)	21 (55)
Heartburn, N (%)	12 (32)
Gastroesophageal reflux disease, N (%)	11 (29)
Endoscopic features	
Furrows, N (%)	11 (29)
Rings, N (%)	4 (10)
Furrows and rings, N (%)	12 (31)
White exudate, N (%)	4 (10)
Stricture, N (%)	8 (21)

SD, standard deviation.

was classified as normotensive in 34 (89%) studies, hypotensive in 3 (8%), and hypertensive in 1 (2%).

Of the 38 patients with EoE who underwent HRM, 22 (58%) were found to have esophageal motility abnormality on HRM, and 16 (42%) had normal study. Fourteen (37%) patients had absent peristalsis with pan-esophageal pressurization and normal integrated relaxation pressure (IRP), except for 1 patient with an elevated IRP of 17. The mean IRP was measured at  $9 \pm 4$  mmHg. Within this group of patients exhibiting pan-esophageal pressurization, 10 patients had presented with food impaction requiring endoscopy for disimpaction as well as esophageal dilation ( $P = .015$ ). In 8 of the 38 EoE patients, peristaltic dysfunction with distal compartmentalization was observed (Tables 2 and 3).

Patients with pan-esophageal pressurization underwent aggressive treatment with 40 mg of omeprazole twice daily and 200 mg of topical fluticasone twice daily. Also, these patients were asked to avoid certain products like (milk, wheat, egg, peanut, and soybean) as part of their treatment. Most of these patients were able to

**Table 2.** HRM Results in Patients With Eosinophilic Esophagitis (N = 38)

LES	
Pressure (mmHg) (mean) (SD)	17 (7)
Normotensive, N (%)	34 (89)
Hypotensive, N (%)	3 (8)
Hypertensive, N (%)	1 (2)
Esophageal body	
Pan-esophageal pressurization, N (%)	14 (37)
Peristaltic dysfunction, N (%)	8 (21)
Normal study, N (%)	16 (42)

SD, standard deviation.

**Table 3.** HRM Findings by Food Impaction

	No food impaction, N = 17	Food impaction, N = 21	P
HRM findings			.015 <sup>a</sup>
Compartmentalized distal pressurization	3 (17.6%)	2 (9.5%)	
Fragmented peristalsis	1 (5.9%)	0 (0.0%)	
Normal UES, LES, & esophageal body	9 (52.9%)	7 (33.3%)	
Pan-esophageal pressurization	2 (11.8%)	12 (57.1%)	
Weak peristalsis	2 (11.8%)	0 (0.0%)	

UES, upper esophageal sphincter; LES, lower esophageal sphincter.  
<sup>a</sup>Fisher’s exact test.

discontinue topical steroids after improvement of symptoms in 3–6 months.

Of these patients, 5 underwent both pretreatment and 3-month posttreatment HRM. Assessment of posttreatment HRM revealed disease regression (Figure).

All other patients were treated either with 40 mg of omeprazole daily, or 40 mg of omeprazole twice daily. In addition, patients were asked to avoid dietary products like (milk, wheat, egg, peanut, and soybean).

### Discussion

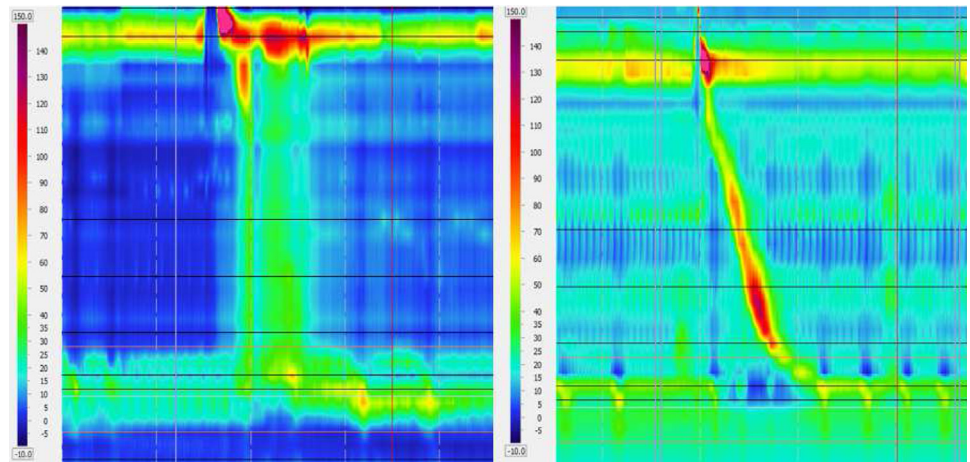
As a relatively new disease that has gained increased prevalence over the last few decades, EoE continues to be further understood. While the endoscopic and histological characteristics of EoE have been established, such as the presence of at least 15 eosinophils per high-power field in the esophageal epithelium,<sup>9,10</sup> the esophageal motility abnormalities of EoE have not yet been clearly elucidated. In this study, we retrospectively assessed HRM findings in patients diagnosed with EoE to correlate esophageal motility patterns with the disease and to delineate relationships between these motility patterns and EoE clinical symptoms.

HRM offers an advantage over conventional manometry by utilizing a sufficient number of pressure sensors in the esophagus, thereby allowing intraluminal pressure to be monitored as a continuum. By positioning pressure sensors

approximately 1 cm apart, few contractile data are lost when generating pressure topography plots for analysis.<sup>3</sup> As for investigating patients with EoE, only a handful of studies to date have employed HRM to evaluate motility patterns in these patients. Results have been variable and have yielded findings such as normal peristalsis, hypomotile disorders, and hypermotile disorders.<sup>11</sup> Some of these studies reported a statistically significant association between EoE and pan-esophageal pressurization after swallowing, compared to control.<sup>6,7,12</sup> Comparable to those results, 58% of EoE patients in our collective exhibited esophageal motility abnormalities on HRM, 37% of which specifically showed pan-esophageal pressurization. With over half of the patients with EoE revealing associated motility pattern irregularities on HRM, our data highlighted that aperistalsis with pan-esophageal pressurization was the most frequently observed esophageal motility abnormality in EoE patients.

In our study, an HRM data analysis indicated that 89% of the EoE patients were considered normotensive for LES pressure, followed by 8% hypotensive, and 2% hypertensive. Importantly, the IRP was under the upper limit of normal for all but 1 patient with pan-esophageal pressurization on HRM. According to the Chicago classification, IRP is measured to evaluate the relaxation of the esophagogastric junction upon swallowing.<sup>13,14</sup> If IRP is elevated to a value above 15 mmHg, patients are classified as having achalasia or esophagogastric junction (EGJ) outflow obstruction; if IRP is normal, peristalsis is then categorized based on factors such as distal

**Figure.** Represents examples of pan-esophageal pressurization at baseline (left) and with improved almost-normal peristalsis after therapy (right).



latency, distal contractile integral, fragmentation, or a complete absence. In patients exhibiting a normal IRP and also have more than 50% of swallows determined to be effective, esophageal motility is defined as normal. With this hierarchical classification scheme in mind, we ruled out impaired EGJ relaxation and functional EGJ outflow obstruction in the 13 of 14 EoE patients in the study due to a normal IRP. However, in 1 patient, IRP was reported at 17 mmHg, and an esophagram revealed the presence of achalasia. It is unclear whether the achalasia was associated with EoE or was an independent event.

While several studies have noted the occurrence of esophageal motility disorders in conjunction with EoE, only a few studies have linked specific motility patterns with the disease. Roman et al<sup>12</sup> suggested a correlation between EoE and pan-esophageal pressurization in the setting of normal EGJ relaxation. Martin et al<sup>7</sup> found similar data through a prospective case-control study. Nennstiel et al<sup>6</sup> also described this association in a prospective observational study and noted that an elevated intrabolus pressure on HRM can be observed in EoE patients compared to patients with reflux or controls. Similarly, our study showed that pan-esophageal pressurization was the most common pattern abnormality identified on HRM in 37% of the EoE patients. Peristaltic dysfunction with distal compartmentalization was detected in 21% of patients, and the remaining 42% of patients had normal studies. This observed pan-esophageal pressurization may be explained by mucosal stiffness resulting from local IgG4-mediated mucosal inflammation.<sup>15</sup> There could be existing fibrosis of the esophageal wall as a sequela of chronic eosinophilic inflammation.<sup>10,16</sup> Alternatively, another possible explanation may be that the presence of overlapping conditions, such as GERD, is contributing to esophageal motor function disturbances.

Furthermore, we also found that of the 14 patients with EoE that displayed pan-esophageal pressurization on HRM, 10 (71%) presented with clinical symptoms of bolus impaction requiring endoscopic intervention. This significant correlation between pan-esophageal pressurization and food impaction corroborates similar findings from the study by Martin et al.<sup>7</sup> Food impaction is a problematic yet common clinical manifestation of EoE. In a Swiss study of 251 patients, 87 patients (35%) experienced 1 or more food bolus impactions that necessitated endoscopic removal.<sup>17</sup> Additionally, Boerhaave syndrome has been reported in cases of undiagnosed EoE where patients induce vomiting subsequent to bolus impaction.<sup>18-20</sup> Patients may also present with hematemesis and esophageal dissection between the mucosal and submucosal layers as a direct result of the endoscopic procedure required for bolus removal and dilation.<sup>21</sup> To limit these complications, efforts should be aimed toward early diagnosis and aggressive treatment of EoE.

Of the study patients with pan-esophageal pressurization, 5 who underwent both pretreatment and posttreatment HRM were identified; all these patients exhibited

regression of disease on posttreatment HRM. These findings are in line with a prospective observational study at a single university center that assessed symptomatic EoE patients who received HRM examinations before and after 8 weeks of topical steroid treatment with budesonide.<sup>6</sup> This study found that 35% of the EoE patients showed abnormal esophageal motility on HRM at baseline, most frequently early pan-esophageal pressurizations resolved after treatment with topical budesonide in 86% of the patients.

In current practice, when a patient presents with clinical symptoms of dysphagia, the initial management usually involves performing an upper endoscopy to rule out the presence of strictures, esophageal carcinoma, or EoE.<sup>13</sup> Following exclusion of these structural abnormalities, manometry can then be used to identify motility disorders of the esophagus. Based on our data indicating a correlation between EoE and esophageal motility abnormalities seen on HRM, and in particular, aperistalsis with pan-esophageal pressurization, we propose that HRM may be utilized as a tool in detecting early progression to pan-esophageal pressurization in patients with suspected EoE.

Early recognition of EoE also entails clinician familiarization with patient demographics, common presenting clinical symptoms, and associated endoscopic features. While EoE can present at any age,<sup>1,22</sup> it has been most frequently diagnosed in atopic males during childhood years, the third decade, or the fourth decade of life. Furthermore, studies have suggested that the disease is more prevalent in non-Hispanic whites.<sup>23</sup> This is consistent with the demographic characteristics of the EoE patients in our study; our study population comprised 74% of white patients and a male-to-female ratio of 2:1 although this ratio is slightly lower than the classically described 3:1 preponderance. Additionally, studies have demonstrated that 50%-60% of patients with EoE have a prior history of atopy.<sup>24-26</sup> In particular, Liacouras et al<sup>23</sup> reported rates of allergic rhinitis and asthma to be 40%-75% and 14%-70%, respectively. While we found that asthma occurred in 24% of the EoE patients, only 18% were noted to have allergic rhinitis. The lower prevalence of allergic rhinitis in our study might be attributed to a smaller sample size or chart documentation errors.

EoE is regarded as a clinicopathologic disease, which requires both symptoms and abnormal histology for diagnosis. Our study showed that the most common symptoms shared by patients with EoE were dysphagia, followed by bolus impaction, heartburn, and GERD symptomatology. These findings bore similarities to previous studies that identified analogous clinical presentations.<sup>9,10,27</sup> However, it is important to consider that clinical symptoms may be underestimated due to underreporting and patient behavioral accommodations, such as avoiding triggering foods and chewing slowly. We also demonstrated that the most common endoscopic feature of EoE patients in the study was furrows and rings, followed by furrows alone, strictures, rings alone, and white exudates. Consistent with our data, several other studies have also confirmed the

presence of similar esophageal abnormalities in EoE. However, none of these findings in isolation are pathognomonic for the disease, as it can appear in various esophageal disorders.<sup>10</sup>

Our study has limitations attributable to a lack of a control group. However, the objectives of this study were to examine esophageal motility patterns on HRM in a group of EoE patients and to establish relationships between these motility abnormalities and clinical symptoms of EoE. Nonetheless, a control cohort with HRM data from patients without EoE may have more explicitly illustrated that the motility pattern encountered is specific to EoE. It also might be interesting to evaluate a larger cohort of patients at multiple centers in future research endeavors to further solidify our assessments.

In conclusion, this study found that of the patients diagnosed with EoE who underwent HRM, more than half had notable esophageal motility dysfunction. Specifically, absent peristalsis with pan-esophageal pressurization in the setting of normal IRP was the most common motility pattern revealed in these patients. Moreover, this abnormality was significantly associated with bolus impaction, a recognized complication of EoE. Data from this study can be utilized to make clinical practice recommendations for employing HRM as an instrument in the early diagnosis of EoE and the prevention of progression to pan-esophageal pressurization and correlated complications. Prompt intervention in patients exhibiting such motility abnormalities may limit episodes of food impaction and ultimately improve patient quality of life.

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Ahmad Abulawi: Conceptualization, methodology, investigation, data curation, writing – original draft. Jacqueline Liu: Conceptualization, methodology, investigation, data curation, writing – original draft. Shawn Philip: Conceptualization, methodology, investigation, data curation, writing – original draft. Mathew Josephson: Conceptualization, methodology, investigation, data curation, writing – reviewing and editing. Hala Abdelwahab: Conceptualization, methodology, investigation, data curation. Paul J. Feustel: Data analysis. Asra Batool: Conceptualization, methodology, investigation, data curation, supervision, project administration, writing – review and editing. All authors had full access to all the study data and have read and approved the final manuscript, analysis, and interpretation of data.

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The corresponding author, on behalf of all authors, jointly and severally, certifies that their institution has approved the protocol for any investigation involving humans or animals and that all experimentation was conducted in conformity with ethical and humane principles of research.

**Data Transparency Statement:**

The data, analytic methods, and study materials will be made available to other researchers upon request.