Summary

Dysphagia, heartburn, and regurgitation are common esophageal symptoms, affecting nearly half of the US population. The diagnostic armamentarium has significantly evolved over the last 3 decades with the advent of high-resolution esophageal manometry (HRM) and functional luminal imaging probe (FLIP) for studying esophageal motor function. In this review, Patel and colleagues discuss the current approach to diagnosis and therapeutics of various esophageal motility disorders. They then provide details about currently available diagnostic tools and discuss both the evaluation and management of disorders of the esophagogastric junction (EGJ) and esophageal peristalsis. Lastly, they discuss the effects of esophageal mucosal diseases, systemic disease, and medications, and altered foregut anatomy on esophageal motility.

Diagnostic tools

Esophagogastroduodenoscopy is required for evaluating patients with suspected esophageal dysmotility because it allows direct mucosal visualization and excludes benign (e.g., peptic stricture, hiatal hernia, Schatzki’s ring, eosinophilic esophagitis, altered foregut anatomy) or malignant conditions that can lead to secondary motility abnormalities. HRM is the gold standard diagnostic tool for esophageal motility disorders and Chicago Classification v4.0 is used for specific manometric classification. FLIP is the newest FDA-approved diagnostic tool, but still in early clinical phases. It complements HRM in diagnosing manometric EGJ outflow obstruction or inconclusive pattern. An EGJ distensibility index < 2 mm²/mmHg is considered definitely abnormal, whereas an EGJ diameter of < 13 mm is likely abnormal. A timed barium esophagram (TBE) with a 13-mm tablet serves as a less expensive and widely available alternative to evaluate esophageal emptying at 1, 2, and 5 minutes. Barium column height > 5 cm at 1 min or > 2 cm at 5 minutes suggests outflow obstruction (such as achalasia).

Disorders of esophagogastric junction

Achalasia: Accurate manometric subtyping of achalasia allows better tailoring of the available treatment options. The 3 first-line treatment options are per-oral endoscopic myotomy (POEM), pneumatic dilation, and laparoscopic Heller myotomy. All have equal efficacy for type I or type II achalasia, but POEM is preferred for type III achalasia due to the ability to perform a tailored longer myotomy. POEM is associated with higher rates of postmyotomy reflux. In patients who are not definitive candidates for any of the 3 first-line options, endoscopic botulinum toxin injection is preferred.

EGJ outflow obstruction: Clinically conclusive diagnosis requires: 1) conclusive manometric diagnosis, 2) appropriate symptom presentation with either dysphagia and/or noncardiac chest pain, and 3) confirmation of findings with signs of outflow obstruction on supportive testing (either FLIP or TBE). A majority (52%–92%) of patients with mild symptoms have spontaneous resolution. For those requiring therapy, botulinum toxin injection to the lower esophageal sphincter and/or endoscopic dilation are favored as first-line options.

Clinical Practice Take-Home Points

• High-resolution esophageal manometry is the gold standard tool for diagnosing esophageal motility disorders. Functional luminal imaging probe and timed barium esophagram serve as complimentary tests for manometric EGJ outflow obstruction or inconclusive manometry pattern.

• Per-oral endoscopic myotomy (POEM), graded pneumatic dilation, and laparoscopic heller myotomy are 3 first-line treatment options for patients with achalasia. POEM is preferred for type III and is associated with higher rates of postmyotomy reflux.

• In patients with disorders of esophageal peristalsis such as distal esophageal spasm, hypercontractile esophagus, ineffective esophageal motility, or absent contractility, evaluation for underlying reflux should be the first step. Subsequently, treatment should be focused on the predominant symptom (dysphagia and/or non-cardiac chest pain).

• Opioid medications are associated with spastic disorders of the esophageal body. If feasible, opioid withdrawal should be the first step as this potentially reverses the motility abnormality.
Disorders of esophageal peristalsis

This includes spastic motor disorders (distal esophageal spasm or hypercontractile esophagus) and hypomotility disorders (ineffective esophageal motility or absent contractility). Treatment approaches vary. The review outlines an approach that first stratifies management on whether or not gastroesophageal reflux disease is an underlying feature. If not, specific treatment (eg, pharmacologic or endoscopic) is predicated on the prominent bothersome symptom (ie, dysphagia or non-cardiac chest pain).

Figure 1. Manometric classification of various esophageal motility disorders based on Chicago Classification v4.0. HRIM (high-resolution impedance manometry); IRP (integrated relaxation pressure); DCI (distal contractile integral); DES (distal esophageal spasm); IEM (ineffective esophageal motility); TBE (timed barium esophagram); FLIP (functional luminal imaging probe).
Figure 2. Treatment options in patients with disorders of esophageal peristalsis after a careful endoscopy is performed to rule out a mechanical or mucosal disease (ie, eosinophilic esophagitis). *In patients with chest pain as the primary symptom, overlapping esophageal hypersensitivity might play a major role in symptom generation and neuromodulators or behavioral treatments might be beneficial based on studies on non-cardiac chest pain.
Summary

The symptoms of eosinophilic esophagitis (EoE) are not accurate for identifying patients in histologic remission, but the reasons for this disconnect are not well explored.

Safroneeva and colleagues recently performed a prospective study of adults with EoE enrolled in a multisite, prospective Consortium of Gastrointestinal Eosinophilic Disease Researchers (CEGIR) OMEGA observational study (NCT02523118). Patients completed the symptom-based EoE activity index (EEsAI) patient-reported outcome instrument as well as other validated instruments for the assessment of biologic disease activity and underwent endoscopy with biopsies. The authors examined the relationship between biologic findings including esophageal eosinophilia (eos/high-power field [hpf]) and symptoms in 3 groups of patients: patients that never underwent dilation, and patients that underwent dilation in ≤ 12 months or > 12 months prior to completing the study questionnaires and undergoing endoscopy.

Among 100 patients (n=61 men, median age 37 years), 15 and 40 patients underwent dilation ≤ 12 months and > 12 months before the index endoscopy, respectively. In nondilated patients, the association between eos/hpf and symptoms was moderate (Spearman’s Rho=0.49, P < .001); for a 10 eos/hpf increase, the predicted EEsAI increased by 2.69 (P = .002). In patients dilated ≤ 12 and > 12 months before the index endoscopy, this association was abolished (Spearman’s Rho=-0.38, P = .157 for ≤ 12 months and Rho=0.02, P = .883 for > 12 months); for a 10 eos/hpf increase, the predicted EEsAI changed by -1.64 (P = .183) and 0.78 (P = .494), respectively.

Dilation modifies the association between symptoms and eos/hpf (P = .005 and P = .187 for interaction terms of eos/hpf and dilation ≤ 12 months and > 12 months before the index endoscopy, respectively).

Clinical Practice Take-Home Points

- Symptoms are not accurate for predicting histologic remission in EoE. Due to this disconnect between biologic findings and symptoms, endoscopy with biopsy is recommended for follow-up of adult EoE patients to assess esophageal inflammation that, if persists, leads to stricture formation over time.

- In nondilated EoE adults, esophageal eosinophilia correlates moderately with symptoms; this correlation was no longer evident in dilated patients, and the dilation effects lasted longer than 1 year. Similar data were observed when the relationship between the endoscopic reference score and symptoms was examined.

- The results of this study should be cautiously interpreted. Only limited information about dilation characteristics was collected; dilator type, diameter achieved in a single session, and number of sessions were unknown. The study describes a 25% subset of the cohort, as remaining enrolled patients were excluded due to missing data. The study findings are also susceptible to bias as they are based on a small number of patients.

- Based on previous data, demonstrating symptom improvement that reflects improvement in esophageal eosinophilia in dilated patients might prove futile, and symptom severity in dilated patients at study baseline does not reflect their inflammation level. Although dilated patients benefit from anti-eosinophil therapies, physicians should not rely on symptoms alone for monitoring and assessing treatment responses in dilated patients. Dilation effects last longer than 12 months.
Figure 1. Scatter plots of (A) EEsAI vs eos/hpf, and (B) EEsAI vs EREFS in nondilated patients (n = 45), in patients dilated > 12 months (n = 40), and ≤ 12 months (n = 15) before index endoscopy. The marginal effects plot of expected EEsAl in nondilated patients (n = 45), in patients dilated > 12 (n = 40) and ≤ 12 (n = 15) months prior to index endoscopy by eos/hpf (C), and by EREFS (D).

In nondilated patients with the peak eos/hpf of 50 and 100, values of predicted EEsAl of 33 and 47, respectively, are observed. In patients dilated < 12 months of index endoscopy with the peak eos/hpf of 50 and 100, values of predicted EEsAl of 20 and 12, respectively, are observed. EEsAl, eosinophilic esophagitis activity index; EoE-QoL-A, adult eosinophilic esophagitis-specific quality of life; eos/hpf, eosinophils per high-power field; EREFS, endoscopic reference score; PRO, patient-reported outcome.