Anatomic and Physiologic Tests of Esophageal and Gastric Function

4

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Introduction

Both the medical and surgical management of chronic and acute disease require an accurate diagnosis and understanding of the underlying physiology and pathology. Physiology is often thought of in global terms, but scientific discovery and innovation over the last millennia have enabled the scientific community to accurately describe, quantify, and manipulate human physiology in a way that allows clinicians to tailor treatment plans and interventions in an individual fashion.

The foregut is at the forefront of intestinal transit and motility as well as digestion and absorption. Thus the manipulation of these processes during the treatment of disease, both medically and surgically, allows for both treatment success and treatment consequences. This chapter will review the various methods for the evaluation of esophageal and gastric transit, motility, acid physiology, as well as anatomic considerations and evaluations. It will review the basic procedural elements to each testing method and review salient features to each test.

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Esophageal Motility

Barium Swallow

The barium esophagram is a useful diagnostic tool in the real-time evaluation of esophageal anatomy, motility, and physiology. It is often the initial test used in the evaluation of dysphagia given its ability to identify both mechanical and functional causes, but it is also widely used in the evaluation of gastroesophageal reflux disease, hiatal hernias, peristalsis, and postoperative functional and structural evaluations. A barium swallow is used in patients with a suspected proximal esophageal lesion such as Zenker's diverticulum or stricture, both of which may carry a risk of perforation with initial evaluation by upper endoscopy. It is also used following an unrevealing upper endoscopy when a subtle mechanical obstruction is still suspected. Though high-resolution manometry and impedance technology are now commonly available for assessment of esophageal motility and bolus transit, the barium esophagram can be used in conjunction with these tests for further evaluation and confirmation.

Basic Procedure Prior to performing the barium esophagram, the patient should have nothing by mouth for 2 h. The exam begins by examining the pharynx and upper esophageal sphincter in the upright lateral and anteroposterior (AP) positions. Esophageal emptying is assessed in the upright positions. If esophageal emptying is impaired in the upright position, the exam is then converted to a timed barium swallow to assess for the possibility of achalasia. Spot images of the esophagus are obtained at 1, 2, and 5 min with times denoted on the image [1]. The gastroesophageal junction (GEJ) and the air-fluid column should be included in each image. In a normal individual, the barium should empty within 1 min. This timed study can be used to confirm an achalasia diagnosis or used after treatment to monitor success of treatment and detect disease [2].

If esophageal emptying is normal in the upright position, then the exam continues with the double-contrast portion. The patient is placed in the erect left posterior oblique position and swallows a sodium bicarbonate effervescent agent dissolved in 10 cc of water in order to distend the esophagus. This is followed by rapidly swallowing of 2 ounces of "thick" (high-density) barium, and spot images are obtained to assess the esophageal mucosa.

To observe the motility phase without the effect of gravity, the patient is then placed in the horizontal right anterior oblique position and is asked to swallow single sips of "thin" (low-density) barium. Three to five individual sips should be observed, as motility disorders can be intermittent. The patient then drinks the barium continuously to fully distend the esophagus, and then single-contrast spot images of the entire esophagus are obtained. This distention is useful to detect strictures, rings, and contour abnormalities from extrinsic compression and to evaluate the GEJ [3].

Gastroesophageal reflux is then assessed. The patient is rolled into the left lateral position to allow barium to move into the gastric fundus. Then the patient is observed as he or she is rolled into the right posterior oblique position. If no reflux is seen, several maneuvers can be used to provoke gastroesophageal reflux including the Valsalva maneuver, strong cough, and the water siphon test. The degree of esophageal injury depends on the amount of reflux, the superior extent of the reflux, and the time it takes to clear. The sole purpose of the barium swallow is not to determine the presence or absence of reflux but to assess for the complications from reflux (strictures, erosions, hiatal hernias). As compared to pH and impedance monitoring in the evaluation of reflux, barium esophagography is the only method available to measure reflux volume.

A 13 mm barium tablet is given to patients with dysphagia unexplained by the findings on the routine study or to evaluate possible strictures and assess its clinical significance. The barium tablet can be used to localize the site of subtle obstruction such as a ring or stricture that the patient could have compensated for in earlier tests by smaller and slower ingestion of liquids. Barium meals can also be useful in order to provoke the patient's symptoms. This form of provocative testing can help distinguish the actual site for symptom development in patients who may have more than one potential contributor.

Motor Function/Peristalsis Esophageal peristalsis normally occurs in three distinct phases which can be elicited and observed using the barium esophagram. With intake of a bolus, the upper esophageal sphincter (UES) relaxes allowing the bolus to pass from the pharynx to the cervical esophagus. A primary peristaltic wave then occurs with the contraction of the inner circular muscles and propagation of the contraction to the distal esophagus. During normal peristalsis the barium column will rapidly progress distally as an inverted *V* [4]. This coordinated and stepwise progression down the esophageal body results in a primary stripping wave that can be observed on barium esophagography. The lower esophageal sphincter (LES) then relaxes and allows the bolus to pass through the GEJ into the stomach. A secondary peristaltic wave, which is induced by esophageal distention from any retained barium bolus or refluxed material, may occur in up to 30% of normal swallows and clears any remaining bolus without the need for an additional swallow triggered by a conscious effort [5]. Tertiary contractions are simultaneous, isolated, and dysfunctional contractions with no peristaltic or physiologic function. Barium esophagography can also be used to visualize "proximal escape," in which a small volume of barium escapes proximally from the inverted *V* to an area previously cleared. This can be a normal variant and is typically cleared by secondary peristalsis; however, substantial (>10 cm) retrograde escape has also been shown to be due to hypotensive peristaltic waves in patients with incompetent peristaltic contractions or occurring prior to the next swallow due to obstruction [6]. Proximal escape can also result from breaks in the peristaltic wave, typically occurring in the transition zone between the striated muscle of the proximal esophagus and the smooth muscle distally. These peristaltic breaks may appear as an incomplete stripping wave during peristalsis evaluation.

Motility Disorders

With the capability of assessing bolus transit and structural characteristics with fluoroscopy, the barium swallow can aid in the diagnosis of motility disorders. Classical achalasia (type I), characterized by failure of LES relaxation and aperistalsis, may show a smooth taper of the esophageal lumen toward the LES, giving the classic "bird beak" appearance. A dilated and tortuous esophagus may be seen proximally along with aperistalsis of the lower two-thirds of the esophagus, and delayed barium emptying (Fig. 4.1) [3]. It is important to note that a barium esophagram cannot always distinguish between primary achalasia and secondary achalasia, and thus direct endoscopic evaluation as well as esophageal manometry should be used as conjunctive studies [7]. Also, if esophageal manometry shows equivocal results, an esophagram should be performed to assess esophageal morphology and emptying [8].

Spastic esophageal motility disorders may be seen on a barium esophagram as lumen-obliterating contractions or tertiary contractions seen during peristalsis evaluation in the setting of distal esophageal spasm or hypertensive peristalsis. Distal esophageal spasm can have a "corkscrew appearance" as the esophagus is compartmentalized with repetitive and simultaneous lumen-obliterating contractions (Fig. 4.2) [9]. Secondary esophageal motility disorders such as those due to scleroderma, diabetes mellitus, or gastroesophageal reflux disease may be characteristically identified and suggested with fluoroscopy. In patients with scleroderma, the GEJ is often patulous with free gastroesophageal reflux. Barium may be ineffectively cleared due to poor LES tone and ineffective contractions

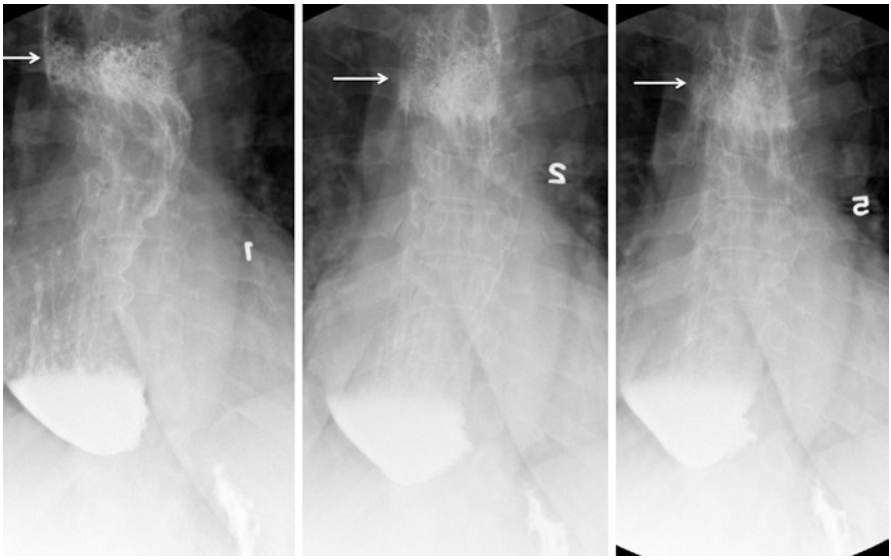

Fig. 4.1 Timed barium esophagram at 1, 2, and 5 min demonstrates a static column of fluid (arrow) within the dilated esophagus and a birds beak appearance of the lower esophageal sphincter. This is a classic appearance of type 1 achalasia

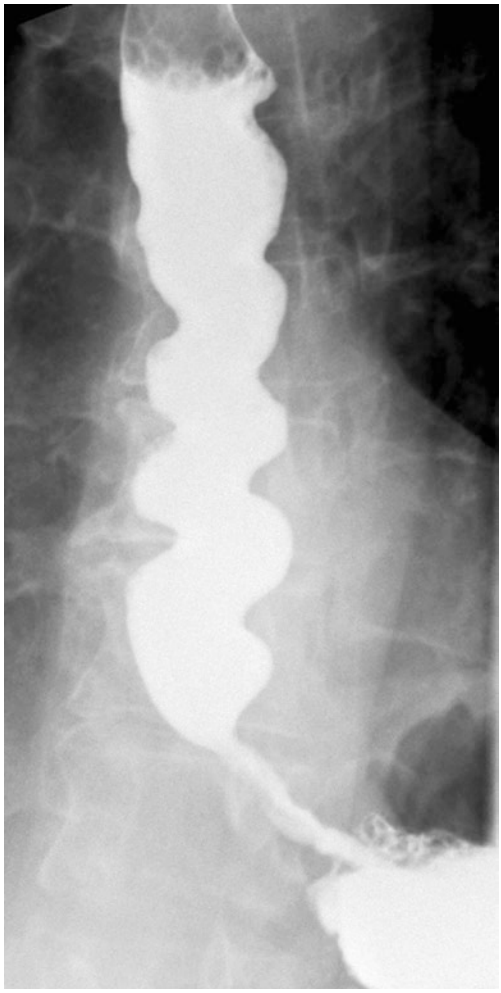

Fig. 4.2 Single-contrast barium esophagram in a patient with distal esophageal spasm shows tertiary contractions throughout the mid and distal esophagus. The contractions delay emptying of the esophagus

from atrophied smooth muscle in the distal esophagus. Patients with scleroderma are at particularly high risk of esophageal stricture formation due to persistent reflux [4, 10].

Anatomic Considerations

Barium esophagography evaluates structural components of the esophagus that may be contributing to symptoms of dysphagia such as strictures, rings and webs, ulcers, hernias, diverticula, and neoplasms. The double-contrast barium esophagram allows for enhanced mucosal evaluation and provides detail for diagnosing mucosal pathology. Radiographic findings of esophagitis are typically seen in the distal one-third of the esophagus. Findings can include granularity of the mucosa (due to edema and inflammation), fold thickening, erosions, ulcerations, and stricture [11]. Barrett's esophagus, a premalignant complication of GERD, may be suggested on barium

testing as a delicate reticular pattern in the distal esophagus or as a stricture in the mid-esophagus, although endoscopy and histology are still required for diagnosis [12, 13]. GERD may also be suggested by the presence of a "feline esophagus" where transient transverse folds are present in the distal esophagus on barium esophagography (Fig. 4.3a).

The barium esophagram allows for a more accurate diagnosis of esophageal rings and webs, as these can be subtle and overlooked by endoscopy. Esophageal webs may be seen in the cervical esophagus, often occurring anteriorly and are usually eccentric. The esophageal vestibule is bordered superiorly by the muscular "A" ring and inferiorly by the mucosal "B" ring at the squamocolumnar junction (Fig. 4.3b). A Schatzki's ring is a weblike narrowing of the "B" ring that causes dysphagia. The "B" ring is located at the EGJ and is a thin concentric protrusion covered by squamous epithelium proximally and gastric columnar cells distally (Fig. 4.3c). A "C" ring may also be identified, and this denotes a ring formed by diaphragmatic crural pressure. A "ringed" esophagus has been described as multiple circumferential rings occurring most commonly in the mid-esophagus and is associated with eosinophilic esophagitis (Fig. 4.3d) [14].

Identification of the GEJ on the barium swallow is important to diagnose a hiatal hernia. Inspiration while lying prone can accentuate subtle sliding-type hiatal hernias (Fig. 4.3e). The barium swallow can characterize and subtype hiatal hernias. Identification of a shortened esophagus is critical in the preoperative evaluation of patients with GERD as it may alter surgical planning [15, 16]. Esophageal diverticula can also be identified with barium swallows.

In the immediate postoperative exam, water-soluble contrast can be used to assess for leak. Postoperative barium swallows may also be helpful to assess to integrity and position of the fundoplication wrap as well as for recurrent hiatal hernia [17].

Esophageal Manometry

The evaluation of esophageal motility, in a dynamic fashion, was initially only able to be completed with the barium esophagram. With the advent of esophageal pressure monitoring in the 1940s, scientists have had an additional method to clarify and quantify esophageal motility in both health and disease. Catheters, placed transnasally into the stomach, were initially water-perfused and had between four and eight pressure sensors that were spaced apart every few centimeters. Each of these sensors is connected to a transducer and an external data recording device which allows pressure amplitudes to be logged and displayed over time in a continuum along the esophageal body. This technology has been largely replaced by high-resolution esophageal manometry (HRM) which utilizes pressure monitors in a solid-state catheter which are spaced out approximately every 1 cm. (Fig. 4.4). There are numerous brands and configurations, but most esophageal catheters have between 32 and 36 sensors which allow for a more detailed analysis of both the esophageal body and the LES than was previously seen with conventional manometry. The resultant pressure tracings are converted to Clouse plots, termed

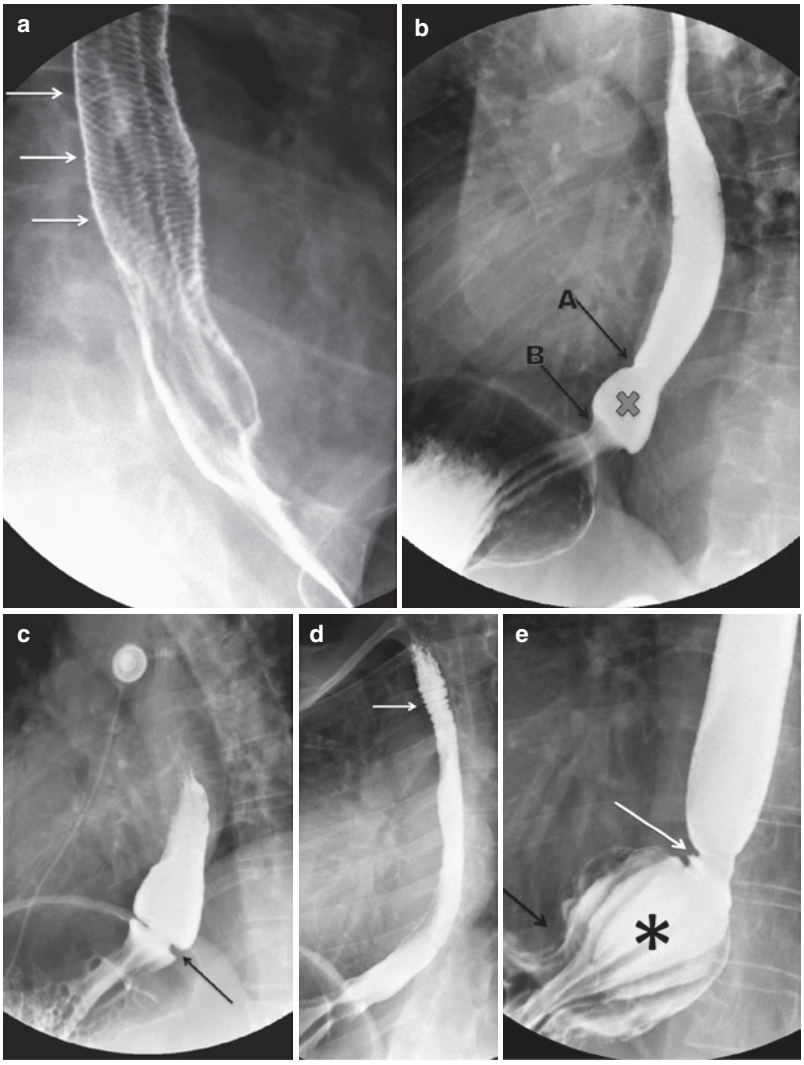

Fig. 4.3 (**a**) Top left**,** double-contrast barium esophagram demonstrates thin, transient transverse folds in the distal esophagus, consistent with "feline esophagus." This appearance is almost always consistent with gastroesophageal reflux and occurs transiently in response to reflux. (**b**) Top right, GEJ anatomy: right anterior oblique image of a barium filled esophagus in a patient with a normal gastroesophageal junction. "A" designates the muscular A ring. "B" designates the mucosal B ring. "X" designates the esophageal vestibule. (**c**) Bottom left, Schatzki's ring: right anterior oblique image of the gastroesophageal junction in a 42-year-old man with dysphagia. The B ring narrows the gastroesophageal junction to 1 cm and is the cause of the patient's dysphagia. This Schatzki's ring prevented the passage of the barium tablet. (**d**) Bottom center, single-contrast barium esophagram image obtained in the right anterior oblique position in a patient presenting with dysphagia shows a "ringed" appearance of the upper thoracic esophagus *(arrow)* where there is mild narrowing. This was confirmed to represent eosinophilic esophagitis. (**e**) Bottom right, hiatal hernia: this is a 49-year-old woman with history of reflux and increasing dysphagia. A peptic stricture is present at the gastroesophageal junction *(white arrow)*. The patient has a sliding-type hiatal hernia *(black star)*. The hiatus is widened in the patient *(black arrow)*, making her more prone to reflux

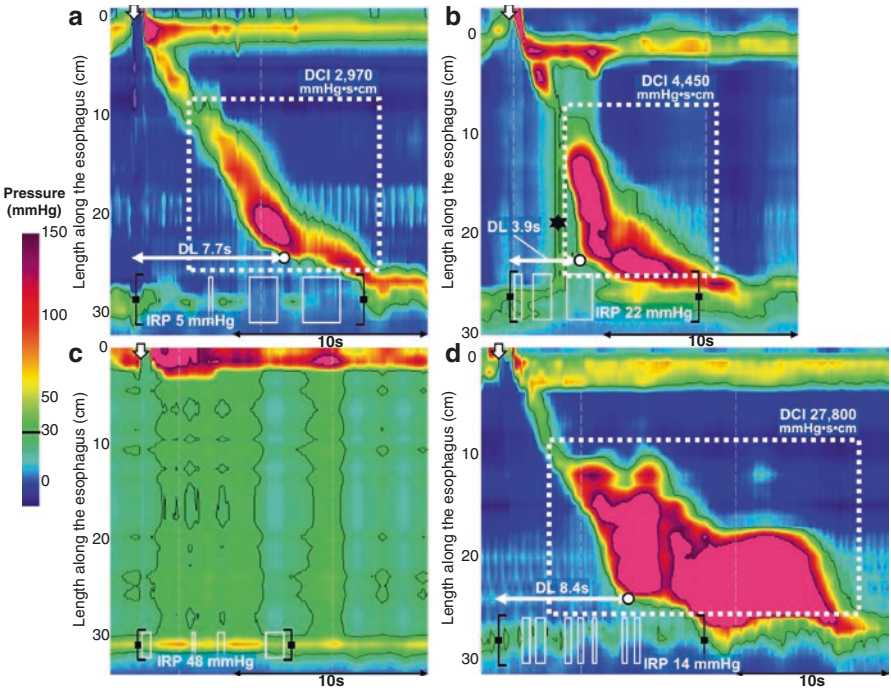

Fig. 4.4 High-resolution esophageal manometry metrics: examples of (**a**) a normal swallow, (**b**) a premature swallow, (**c**) a failed swallow with pan-esophageal pressurization, and (**d**) a hypercontractile swallow are displayed. Swallow onset (relaxation of the UES) is represented by a white arrow. The contraction deceleration point is represented by a white dot. Compartmentalized pressurization (star) can be appreciated in B. DCI, distal contractile integral; DL, distal latency; IRP, integrated relaxation pressure. (From Kahrilas [88])

esophageal pressure topography, which display a vivid representation of pressure amplitude over time and space [18]. The HRM computer software also allows for a virtual sleeve to be created to accurately characterize the LES by grouping 5–6 sensors together in the distal esophagus.

The manometry catheter can be placed transorally but is typically placed transnasally due to patient tolerability. The catheter is passed down the esophagus and positioned across the LES, 2–3 cm into the stomach. The study is typically performed in the supine position, similar to barium esophagography, to reduce the effects of gravity and allow for isolated measurement of esophageal peristalsis and motility. Either before or after the assessment of esophageal peristalsis, baseline characteristics of the esophagus are recorded including basal/resting LES and UES pressures, the presence or absence of a hiatal hernia, and the relationship between the LES and diaphragm. To evaluate peristalsis, the patient is given 5 cc boluses of saline, separated by at least 30 s between swallows to allow for a return of baseline muscle potential. Typical protocols involve the recording and analysis of ten individual swallows. Variations can be

performed, including the use of viscous or solid foods instead of saline or using the semi-erect or erect posture depending on patient tolerability of the supine position.

High-resolution manometry testing provides quantifiable, objective measurements which allow for standardized interpretation. The Chicago Classification for Esophageal Motility Disorders, currently in its third edition, is the most widely used classification scheme for defining esophageal motility disorders [19] (see Chapter 32). This system utilizes an approach in which each swallow is analyzed with regard to esophageal body contraction vigor, esophageal contraction pattern, LES relaxation, and the intrabolus pressure pattern (Table 4.1).

The contraction vigor of esophageal peristalsis is measured by a software algorithm of the contraction pressure from the start of the transition zone, where the esophageal muscle composition changes from striated to smooth muscle, to the LES (Clouse segments 2 and 3) [18]. This is termed the distal contractile integral (DCI) and is measured in terms of mmHg × cm × s. Normative values for the DCI and the other definitions listed below have been suggested by the International HRM Working Group and are based on studies primarily performed on the Medtronic (formerly Sierra Scientific) apparatus [19]. Contraction vigor is defined as weak

Table 4.1 Esophageal manometry keywords and measurements

Keyword	Definition	Application
Distal contractile integral (DCI)	The contraction pressure (measured by mmHg × cm × sec) from the start of the transition zone to the LES	Failed contraction (DCI <100) Weak (DCI <450) Normal (DCI 450–8000) Hypercontractile (DCI >8000)
Contractile deceleration point (CDP)	The inflection point where propagation velocity slows as it approaches the LES at the phrenic ampulla	Allows for measurement of distal latency
Distal latency (DL)	The time interval (measured in amplitude × duration × length) between UES relaxation and the peristaltic wave reaching the CDP	Normal >4.5 s Premature contraction is <4.5 s Helps define distal esophageal spasm and type III achalasia
Peristaltic breaks	Gaps in the 20 mmHg isobaric contour of the peristaltic contraction between the UES and EGJ, measured in axial length	Swallow is termed "fragmented" if breaks are present >5 cm in length
Integrated relaxation pressure (IRP)	The average lowest EGJ pressure measured for 4 contiguous or noncontiguous seconds of relaxation in the 10 s window following deglutitive UES relaxation	Normal IRP < 15 mmHg Impaired EGJ relaxation is an IRP >15 mmHg which is a defining characteristic of achalasia
Esophageal pressurization	Intrabolus pressure measurement within the esophagus	Normal: No bolus pressurization >30 mmHg Panpressurization: Uniform pressure > 30 mmHg from UES to EGJ Compartmentalized: pressurization extending from contractile front to EGJ

(DCI <450), failed (DCI <100), hypercontractile (DCI >8000), or normal (DCI 450–8000). Similar metrics have been defined on other platforms [20, 21].

To evaluate for premature contractions, the time interval between UES relaxation and the peristaltic wave reaching the contraction deceleration point (CDP) is measured. The CDP demarcates the inflection point where esophageal peristaltic velocity slows as it approaches the LES at the esophageal vestibule [22, 23]. This time elapse is termed the distal latency (DL), and normal values have been determined for each of the software apparatuses [20, 21, 24]. Swallows with a value less than 4.5 s are considered premature. This metric is primarily used in defining distal esophageal spasm and type III achalasia (see Chapter 31).

When evaluating the LES, the metric used to define appropriate deglutitive EGJ relaxation is called the Integrated Relaxation Pressure or IRP. The IRP, measured in mmHg, is the average lowest pressure in four contiguous or noncontiguous seconds of deglutitive relaxation in the 10-s relaxation window which begins at UES relaxation. This metric is expressed as the median value of the 10 analyzed swallows and is normal if <15 mmHg on the Medtronic apparatus. Impaired LES relaxation is defined as an IRP >15 mmHg (>20 mmHg on Sandhill software), and this is one of the defining characteristics of achalasia.

Breaks in peristalsis, where circular muscle contractions do not occur contiguously, can be seen on esophageal pressure topography. Breaks are considered clinically significant if they are greater than 5 cm in axial length. If present, these swallows are termed fragmented and may be associated with impaired bolus transit [19, 25]. Intrabolus pressurization patterns are also defined by the Chicago Classification [19]. Pressurization within the esophagus greater than 30 mmHg is considered abnormal and is classified into "panpressurization" if this occurs from the UES to the EGJ or "compartmentalized" if this extends from the contractile front to the EGJ.

Each swallow is analyzed individually based on the above parameters, and then the Chicago Classification is applied to determine if a major or minor disorder of peristalsis is present. Also, the presence of a hiatal hernia can be determined as well as characteristics of EGJ morphology. When esophageal manometry is coupled with impedance monitoring, bolus transit abnormalities can also be described.

Assessment of Esophageal Bolus Transit

Clinically, patients with dysphagia will often describe the sensation of food "sticking" or slowing in their neck, chest, or epigastrium. Dysphagia symptoms may also develop after esophageal or gastric surgery. In addition to describing esophageal peristalsis and motor function, assessment of bolus transit through the esophagus may also provide clinically useful information. To describe and quantify this, multiple diagnostic methods have been developed including fluoroscopy, luminal impedance testing, and scintigraphy. Each of these tools has different characteristics which provide insight into transit time, the direction of flow, and potential quantification of bolus retention or reflux.

Fluoroscopy

The barium swallow is the gold standard for assessing esophageal bolus transit. It is useful in evaluation of bolus transit and has been shown to have excellent correlation with impedance monitoring [5]. Bolus transit can be assessed in both the erect and horizontal positions. In addition to assessment of bolus transit of liquid barium, the patient can also be tested with provocative foods coated in barium. In patients with a major motility disorder such as achalasia or scleroderma, a barium esophagram may be useful to assess bolus transit because of the low baseline impedance values [26].

Intraluminal Impedance Testing

Impedance is the effective resistance of an electrical circuit. Intraluminal esophageal impedance testing measures the changes in resistance over time due to the conductance of a substance as it passes through the esophagus [27]. Data is gathered via a catheter which has metal electrodes which are positioned at 3, 5, 7, 9, 15, and 17 cm above the GEJ [27]. Changes in impedance, when measured in a sequential fashion, can determine the direction and time of bolus transit without the use of radiation. Impedance monitoring can detect both air and liquid as these substances change the electrical conductivity along the catheter. The baseline impedance of the esophagus is lowered as liquid-containing boluses pass each sensor due to increased ion conductivity, whereas air has high impedance due to poor conductivity [27]. A decrease in impedance from proximal to distal indicates anterograde bolus transit. On the other hand, a change in impedance moving from the distal to proximal esophagus indicates retrograde transit of a refluxed material. A potential limitation of this technology is that liquid boluses of varying volumes may produce similar amounts of changes in impedance within the esophagus; thus, impedance testing cannot be used to accurately measure the volume of swallowed boluses with currently available software. However, preliminary work has been completed using novel, proprietary software, which may allow quantification of bolus transit with this technology [28].

Intraluminal impedance testing is almost exclusively completed on a multichannel device which allows for esophageal motility testing to be completed simultaneously. As previously described, the catheter is placed transnasally down the esophagus into the stomach. Patients are then asked to complete 10 liquid or 10 viscous swallows with each swallow separated by 30 s. The impedance at each electrode is then measured and recorded to show the path and extent of bolus transit. Viscous solutions are important to include in the impedance evaluation as studies have shown that patients being evaluated for nonobstructive dysphagia with normal liquid manometry could actually have a motility disorder as seen by abnormal bolus transit on viscous impedance testing [29–31]. Esophageal transit is deemed abnormal if more than 30% of liquid or 40% of viscous swallows show incomplete bolus transit [28, 32].

Esophageal emptying, as measured by intraluminal impedance monitoring, has been validated against videofluoroscopy with a 97% concordance rate among healthy individuals [5, 33]. The esophageal impedance integral (EII) and bolus flow time (BFT) are additional metrics being evaluated as surrogates for esophageal emptying [28, 34].

Impedance technology has also been applied to the study of gastroesophageal reflux disease as a way to recognize and identify weakly acidic (pH 4–7) and non-acid (pH >7) reflux, which also may contribute to GERD symptoms [35–38] (see combined pH/impedance monitoring).

Esophageal Scintigraphy

Esophageal scintigraphy was initially developed in 1972 and is designed to evaluate esophageal bolus transit in the workup of GERD and nonspecific motility disorders by providing quantitative data on transit through the entire esophagus or in separate regions. In addition, when the scanning area is widened to include the lungs, scintigraphy can help detect episodes of aspiration [39, 40]. Radionucleotide esophageal testing is noninvasive, has a low radiation burden, and is generally well tolerated by patients. After a period of fasting, patients in the upright or supine position are asked to swallow a 10–15 cc bolus, liquid, or in some cases solid, labeled with Tc-99 m sulfur colloid [41]. The volume of radioactive isotopes is detected by a gamma camera. Data are recorded every 0.1–0.15 s and generate time activity curves showing bolus passage time and time to maximal clearance. Normal transit time of a liquid bolus is approximately 7 s in the upright position and 10 s in the supine position, while normal isotope clearance averages 96 percent in either position [42, 43]. Currently, the use of esophageal scintigraphy is limited and may serve in a complementary role to barium swallows and manometry [44].

Physiologic Esophageal Testing

pH Monitoring

Ambulatory esophageal pH monitoring has allowed for easier, more sensitive, and more specific diagnosis of GERD, especially in patients who have failed an empiric proton pump inhibitor trial or those with atypical symptoms. The Tuttle test in 1958 was the first widely used pH test where a probe was inserted into the patient's esophagus and instantly determined the pH to diagnose GERD [45]. As expected, this test had low sensitivity and specificity so in 1974, Johnson and DeMeester performed 24-h pH testing in hospitalized patients [46]. Their research established normal and abnormal standards for esophageal reflux frequency and duration based on a composite score with six parameters: percentage of total time pH < 4, percentage supine time pH < 4, percentage upright time pH < 4, total number of reflux episodes, number of reflux episodes >5 min, and duration of the longest reflux episode.

Thus with baseline values that could be used for more accurate diagnosis, ambulatory pH testing was established in the 1980s [47]. Since then, advancements have been made to pH monitoring, and there are now two widely used methods: catheter-based monitoring and the wireless pH monitor (Bravo™, Medtronic, Minneapolis, MN) [48, 49]. For both methods, prior to placement of the pH monitor, patients should not eat anything after midnight the night before the test. For those patients on proton pump inhibitor or H2 blocker therapy, medications should be stopped for 7 and 3 days, respectively, prior to the test. In catheter-based pH monitoring, the antimony catheter is advanced through the nasopharynx into the esophagus, which can be facilitated by the patient drinking sips of water. The probe is advanced until the pH reads less than 4, indicating entry into the stomach, and then is pulled back so that it rests 5 cm above the LES. The gold standard for pH probe placement is coordinating with esophageal manometry to locate the LES and then pulling the pH catheter back by 5 cm. Some esophageal catheter probes also have proximal sensors to detect acid reflux that may contribute to laryngeal or upper airway irritation. Additionally, an oropharyngeal catheter-based pH probe, Restech (Respiratory Technology Corporation, Houston, TX), is placed in the posterior oropharynx and measures pH of liquid or aerosolized droplets [50]. During the 24-h monitoring period, patients should perform their normal daily activities while keeping a journal indicating the start and end times of meals, any supine positioning, as well as the onset of any symptoms thought to be reflux related. Another technique, wireless pH monitoring, uses the Bravo™ capsule which contains an antimony pH electrode and measures pH at 6-s intervals [48]. As compared to the catheter approach, wireless pH testing is better tolerated by patients and allows for longer testing (up to 96 h) to capture the day-to-day variance in reflux symptoms [48, 51, 52]. The capsule is placed endoscopically 6 cm above the squamocolumnar junction with attachment to the esophageal wall using a special vacuum pump and then communicates by radio transmitter with an external data logger worn by the patient [48]. Typically, the capsule will fall off by itself within 5 days, though the capsule can detach early from esophageal mucosa and enter the stomach, thus recording the acidic gastric contents resulting in a false-positive study.

During the typical 24- to 48-h pH monitoring period, statistical metrics are often used to quantify the association between a patient's symptoms and reflux using three indices: symptom association probability (SAP), symptom index (SI), and symptom sensitivity index (SSI) (Table 4.2) [53–55]. During pH testing, a reflux episode is defined as a drop in pH below 4 that lasts for at least 10 s. The SI is the percentage of reflux-associated symptom episodes [54]. It is calculated by dividing the number of reflux-related symptom episodes by the total number of symptom episodes × 100 and is considered positive if >50% [54]. This index does have drawbacks however as it does not factor in the total number of reflux events. The SSI is defined as the number of symptom-associated reflux episodes divided by the total number of reflux episodes × 100. It is the percentage of symptom-associated reflux episodes and is considered positive if >10% [55]. This metric also has disadvantages as it does not take the total number of symptom episodes into account. The SAP measurement was created to avoid the shortcomings of the SI and SSI by

Table 4.2 Symptom indices for GERD using pH monitoring

Keyword	Definition	Application
Symptom index (SI)	The percentage of reflux-associated symptom episodes Calculation: (# reflux-related symptom episodes)/(# symptom episodes) × 100	Positive if >50% Does not factor in total # of reflux events
Symptom sensitivity index (SSI)	The percentage of symptom-associated reflux episodes Calculation: (# symptom-associated reflux episodes)/(# reflux episodes)×100	Positive if >10% Does not factor in total # of symptom episodes
Symptom association probability (SAP)	The cross-tabulation statistical analysis using the Fisher's exact test of a contingency table consisting of 4 possible combinations of reflux and symptoms (reflux being present or absent and symptoms being present or absent) compiled from the 24-h data divided into consecutive 2-min segments	Created to avoid the shortcomings of the SI and SSI Result ≥95% is considered statistically significant association, though it cannot definitively imply causality

using cross-tabulation statistical analysis of a contingency table consisting of four possible combinations of reflux and symptoms (reflux being present or absent and symptoms being present or absent) compiled from the 24-hr data divided into consecutive 2-min segments [53]. The Fisher's exact test is then used to calculate the probability that the observed distribution of results could have been the result of chance alone or is statistically significant. A result ≥95% is considered statistically significant association, though it cannot definitively imply causality [56]. The SI, SSI, and SAP are typically used in a complementary fashion as direct comparisons may lead to inaccurate conclusions (Table 4.2).

Ambulatory pH monitoring establishes a temporal correlation between symptoms and episodes of reflux, which may be helpful in cases of atypical symptoms of GERD such as cough. Moreover, pH monitoring can stratify patients on the basis of its severity. More severe GERD, which places patients at higher risk for Barrett's metaplasia or other complications, can be seen during pH testing as more acid reflux in the distal and proximal esophagus and slower acid clearance.

Combined pH and Impedance Monitoring

By combining multichannel intraluminal impedance (MII) monitoring with ambulatory pH monitoring, clinicians can characterize the physical properties of the reflux material. MII-pH monitoring can not only determine whether the reflux is acidic (pH <4), weakly acidic (pH 4–7), or non-acid (pH >7), it can also differentiate between gas, liquid, and mixed (liquid-gas) reflux based on impedance values. Additionally, since impedance testing measures reflux independent of pH, a bolus exposure time (BET) is measured which is akin to acid exposure time in pH testing, but it also includes weakly or non-acid reflux [57]. Impedance monitoring also

determines the proximal extent of reflux as there are two impedance channels positioned at 15 and 17 cm above the lower esophageal sphincter. This provides insight into the extent of reflux and may have implications in the management of extraesophageal reflux symptoms. In addition to gastroesophageal reflux disease, MII-pH also has implications in the diagnosis and treatment of other foregut disorders including rumination, aerophagia, supragastric belching, esophageal hypersensitivity, and functional heartburn.

The ability to detect reflux independent of pH helps identify patients with continued symptoms despite PPI therapy. In patients on PPI therapy, the key measurement is the number of acid and non-acid reflux episodes and their relationship with the symptoms using the SI, SSI, or SAP. When patients with persistent symptoms while on acid-suppressive therapy show a positive symptom association between symptoms and reflux, this modality can help the clinician determine if the refractory symptoms are due to uncontrolled acid exposure, ongoing weakly acidic reflux which may denote a hypersensitive esophagus, or if the symptoms are functional in nature. Fundoplication may have a role in the treatment of patients with ongoing reflux and large-volume regurgitation which has been determined to be of weakly or non-acidic in origin as determined by MII-pH testing [56].

Gastric Function and Physiologic Testing

Gastric Emptying

Gastric emptying is frequently assessed in patients with unexplained nausea and/or vomiting, refractory gastroesophageal reflux disease, suspected chronic intestinal pseudo-obstruction, or suspected dumping or stasis syndrome following gastric surgery. Prior to assessing for abnormal gastric emptying, a mechanical obstruction should be excluded with upper endoscopy and/or barium swallow or CT/MRI enterography [58]. In addition, gastric emptying tests can be useful to evaluate response to treatment.

Gastric Scintigraphy Gastric scintigraphy is the most commonly utilized and cost-effective test to evaluate for delayed or rapid gastric emptying. Given the standardization and ease of quantifying gastric retention, scintigraphy has become the gold standard for measuring gastric emptying [58, 59]. A standard test meal is labeled with radioactive isotope, specifically 99mTc for solids and 111 indium for liquids. Ideally, the test meal is standard solid food, usually a low-fat egg-white meal, since liquids will often empty normally from the stomach when solids are abnormally retained and also the fat content of the meal will impact the rate of emptying [60, 61]. Medications that affect gastric emptying should be stopped at least 48 h prior to the test, premenopausal women should have the test done within the first 10 days of their menstrual cycle, and patients with diabetes should have blood glucose checked and hyperglycemia (fasting glucose >275 mg/dL) treated

before the test meal is consumed [58]. After an overnight fasting, the patient ingests the meal within 10 min, and preferably while patient is standing, scans are obtained immediately ($t = 0$) and then 1, 2, and 4 h afterward so that the percentage of gastric emptying can be measured. Anterior and posterior images are obtained to help adjust for depth attenuation as solid food migrates from the posterior fundus to the more anterior gastric antrum and to help distinguish isolated fundal or antral dysmotility. The radioactive counts, expressed as a percent of maximal gastric counts at the beginning of the study, are directly proportional to the volume and amount of solid or liquid remaining in the stomach [62]. Sensitivity for delayed gastric emptying increases over a 4-h evaluation, and thus this time duration is typically preferred over a 2-h evaluation. Delayed gastric emptying using the standard low-fat egg meal is defined as greater than 10% retention of gastric contents at 4 h and/or > 60% at 2 h. Rapid gastric emptying is present when less than 35% or the meal is retained at 1 h [63]. Scintigraphy images may sometimes reveal gastroesophageal reflux. Throughout the evaluation process, it is important to realize that the severity of symptoms does not always correlate with the rate of gastric emptying.

Smart Pill Though scintigraphy is widely used for evaluating gastric emptying, another approach in the ambulatory setting is with the wireless motility capsule, known as the SmartPill™(Medtronic, Minneapolis, MN), which was FDA approved in 2006 for evaluation of gastroparesis. In addition to documenting the time required for the capsule to traverse the gastrointestinal tract via gut peristalsis, the SmartPill™ can simultaneously gather information on phasic pressure amplitudes, temperature, and pH [64]. After an overnight fast, the 26.8 × 11.7 mm SmartPill™ capsule is ingested in conjunction with a standard nutrient bar or meal, and the patient then must fast for the following 6 h to allow for accurate measurement. The SmartPill™ can continue to record data for the transit of the entire GI tract over the next 3–5 days in intervals of 20 s during the first 24 h and every 40 s thereafter. During this time, patients record mealtimes, sleep, and bowel movements, all while avoiding strenuous exercise. Gastric emptying time (GET) is defined as the time of the capsule's ingestion to its departure from the stomach [65]. An abrupt change in pH (pH >4 or ≥ 2 pH units from baseline) signifies the transition from the acidic stomach to the alkaline duodenum to calculate the GET. The SmartPill™ capsule will empty from the stomach with the return of phase 3 of the migrating motor complex, which occurs upon complete emptying of solid food from the stomach [64]. A GET of 5 h or less is defined as normal; a GET greater than 5 h is determined delayed gastric emptying [65]. When comparing the GET simultaneously in healthy and symptomatic patients using scintigraphy and the wireless motility capsule, a strong correlation (>0.7) at 4 h exists between the two tests, suggesting that the capsule method can be a useful determination of clinically significant delayed gastric emptying [66, 67].

Gastroduodenal Manometry

Gastroduodenal manometry, a similar technology to esophageal manometry, can be used to assess the coordination and amplitude of contractions spanning the transition from the gastric antrum to the duodenum. Although this technology is primarily limited to quaternary referral centers and research institutions, gastroduodenal manometry may be used to clarify conditions such as intestinal pseudo-obstruction, partial mechanical obstruction, rumination, gastroparesis, and pylorospasm [68–72]. When dysmotility is suspected, gastroduodenal manometry can help differentiate between myopathic and neuropathic etiologies as myopathic conditions will lead to low-amplitude contractions, while neuropathic disorders will be typically associated with normal to increased amplitude but an unorganized contractile response [71]. From a surgical perspective, gastroduodenal manometry may have the most utility in excluding dysmotility as a contributor to a patient's symptoms and thus can have a major impact on the physician's choice of medical or surgical intervention for patients.

To perform the procedure, patients should fast at least 8 h prior to having one of two different types of motility catheters – water-perfused or solid-state – placed either by endoscopic or nasoenteric placement via fluoroscopic guidance. Antroduodenal motility is recorded in the fasting state for 3 h to assess the 3 phases of the migrating motor complexes. Then, the patient is stimulated, either pharmacologically with erythromycin or octreotide or by meal ingestion, and the postprandial amplitude and frequency of contractions are recorded for an additional hour [3, 73]. Solid-state catheters are typically used because of increased sensitivity due to rapid response to pressure events; in addition, they can now measure contractility patterns over a 24-h ambulatory period. However, it is important to note that these ambulatory results can be affected by motion artifact and vomiting since they can mimic abnormal duodenal contraction patterns or cause the catheter to migrate from its original position [3, 74].

Anatomical Tests

Upper Gastrointestinal Examination

The most common indications for an upper GI include epigastric pain, symptoms of gastroesophageal reflux, anemia, and suspected hiatal hernia. A technique combining double- and single-contrast portions is most commonly used. A single-contrast upper GI study may be used in postoperative settings, immobile patients, in patients with food or fluid in the stomach, or gastric distention (gastric outlet obstruction). The patient should be NPO for 4–6 h before the exam.

The exam begins with the patient in the upright left posterior oblique position. The patient drinks a sodium bicarbonate effervescent agent dissolved in 10 cc of

water followed by 2 ounces of "thick" barium. Three air-distended views of the esophagus are obtained, and then the patient is quickly put in the horizontal position prior to barium entering the duodenum. The patient is rolled to ensure coating of the stomach, and double-contrast images are obtained of the stomach and duodenum. After the double-contrast portion of the exam is over, the patient is then evaluated using single-contrast technique. Esophageal motility is assessed with the patient drinking "thin" barium in the horizontal right anterior oblique position, but videos are generally not recorded in upper GI exams (as they are in barium swallows). Next, single-contrast images of the stomach and duodenum are obtained using paddle compression of the gastric antrum and duodenum. Final spot images are obtained including the stomach, duodenum, and proximal jejunum. Gastroesophageal reflux may then be assessed using provocative maneuvers as previously described.

The gastric cardia is characterized by a stellate fold pattern radiating to the gastroesophageal junction, also known as the cardiac "rosette" [75]. The gastric fundus is defined as the portion of the stomach cranial to the gastric cardia. The gastric body is the portion of the stomach between the gastric cardia and the bend in the mid-lesser curvatures known as the incisura angularis. The gastric antrum is the portion of the stomach extending distal to the incisura angularis to the pylorus (Fig. 4.5) [76]. The rugal folds are most prominent in the gastric fundus and body and are straighter along the lesser curvature and more undulating on the greater curvature. The mucosal surface of the stomach consists of areae gastricae, which are flat polygonal-shaped tufts of mucosa separated by narrow grooves. Enlarged areae gastricae have been reported in the setting of *Helicobacter pylori* gastritis and small or absent areae gastricae have been seen in patients with atrophic gastritis or pernicious anemia [76]. Other pathology seen within the stomach includes rugal fold thickening, erosions, ulcers, polyps, masses, diverticula, or gastric narrowing.

While the esophagus is evaluated in an upper GI exam, images of the pharynx and entire esophagus are not taken with every upper GI exam. Barium swallows are better for the evaluation of dysphagia, gastroesophageal reflux, and esophageal motility, and upper GI exams are better for the evaluation of epigastric pain. Hiatal hernias can be assessed with either exam.

Endoscopy

The advent of fiber-optic endoscopy in the 1950s by Basil Hirschowitz paved the way for focused intraluminal evaluation of the foregut. The esophagogastroduodenoscopy (EGD) is now one of the most commonly performed procedures during the workup and treatment of foregut disorders. Endoscopy is typically performed under moderate sedation or can be performed with deep sedation or general anesthesia with appropriate anesthesia support and personnel.

From an anatomic standpoint, an EGD allows for complete intraluminal visualization of the esophagus, stomach, and proximal duodenum. In the esophagus, the

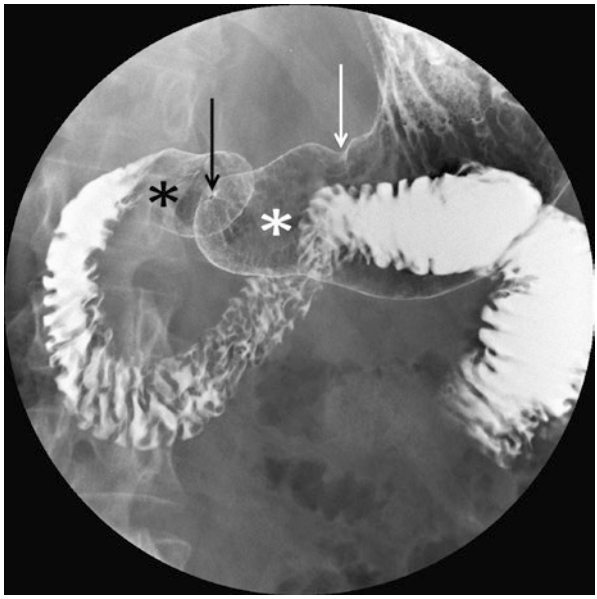

Fig. 4.5 Double-contrast image of the stomach and duodenum. The incisor angularis *(white arrow)* is a bend in the stomach between the lesser curve and antrum *(white star)*. The pylorus is designated by the black arrow and the duodenal bulb by the black star. The normal duodenum has a "C shape" and then extends superiorly to the ligament of Treitz

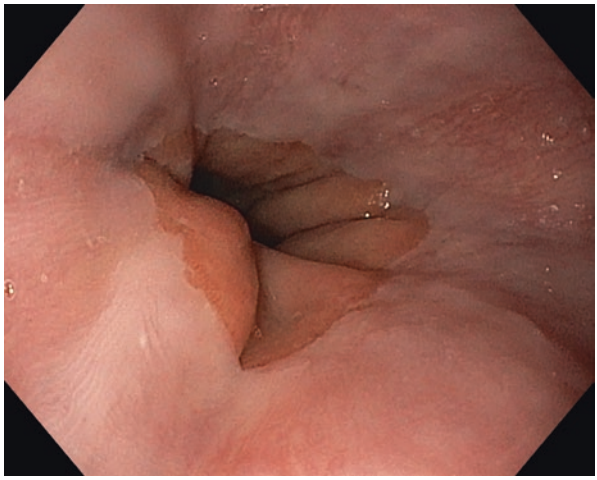

Fig. 4.6 Endoscopic view of the gastroesophageal junction. The white squamous mucosa of the esophagus extends completely to the top of the gastric folds. The GEJ narrows at this level signifying external compression from the diaphragm

presence of complicated gastroesophageal reflux disease can be identified in the form of erosive esophagitis, Barrett's esophagus or stricture. Esophageal tumors, both intraluminal or submucosal, are readily evident on white light endoscopy. The appearance of the GEJ, noted as the transition point between the tubular esophagus and proximal extent of the gastric folds and its relationship to the diaphragmatic hiatus/pinch are easily identifiable (Fig. 4.6). This relationship defines the presence or absence of a hiatal hernia, and retroflexed views of the GEJ/hiatus from within the stomach can help characterize this relationship even further. Classification schemes, including the Hill classification (flap valve), are used to standardize the

reporting of the diaphragmatic hiatus on retroflexed views, and the different grades (Hill/flap valve I–IV) have been shown to directly correlate with the presence and amount of reflux (Fig. 4.7) [77]. Standardized descriptions of the hiatus should be routinely used in endoscopy reports as they can help with operative planning. Endoscopy is also useful in the diagnosis of achalasia or pseudoachalasia as the muscular LES, if not relaxing appropriately, can be felt as the endoscope is passed through the GEJ. Additionally, advanced imaging techniques, such as narrowband imaging (NBI), can be used to better clarify mucosal conditions such as Barrett's esophagus by providing visual contrast during routine endoscopy.

In the stomach, inspection is performed of the body, antrum, incisura, and pylorus, and retroflexed views are utilized for the fundus, cardia, and hiatus. With a typical adult gastroscope, the duodenal bulb and the second/third portions of the duodenum are accessible for inspection, and mucosal sampling is easily performed through the working channel of the endoscope in any location if indicated.

Although endoscopy is not the test of choice for the characterization of upper gastrointestinal motility, it can provide useful information. In the absence of a mechanical obstruction, a dilated esophagus may suggest achalasia, and stasis changes in the form of esophagitis, or retained food/liquid may also suggest hypomotility. Tertiary esophageal contractions may also be visualized in spastic motility disorders. In the stomach, antral contractility is visible, and gross motor dysfunction may be suggested by the presence of retained food/liquid or in the form of a gastric bezoar. Pylorospasm may also be suggested on endoscopy, although gastroduodenal manometry is more specific.

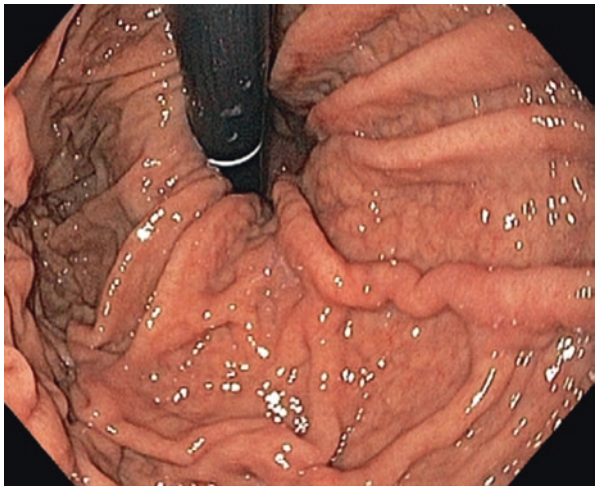

Fig. 4.7 Endoscopic view of an open diaphragmatic hiatus as seen from the retroflexed position. The gastric folds extend cephalad through the hiatus which defines the presence of a hiatal hernia. A muscular ridge is not present. (Hill grade IV flap valve)

Endoscopic Ultrasound

Endoscopic ultrasound (EUS) provides an additional diagnostic dimension to the standard fiber-optic endoscopic evaluation. Performed with an echoendoscope, EUS is indicated in the staging of malignancy for lung, esophageal, GEJ, and gastric malignancies and provides access to structures both within and beyond the luminal wall of the gastrointestinal tract. Submucosal lesions in the esophagus, stomach, and the proximal small bowel can be defined by which layer they originate, and sampling can be performed with fine needle aspiration (FNA). Mediastinal and hilar structures are readily accessible with EUS via the esophagus. When EUS is performed in the stomach and small intestine, the liver, kidneys, adrenal glands, pancreas, biliary tree, and gall bladder as well as adjacent structures (vasculature, lymph nodes, and nerve plexuses) can be characterized based on sonographic features and fine needle aspiration. Although not routinely used in achalasia, EUS can provide additional information regarding the thickness of the inner circular muscles at the level of the LES [78]. In patients with manometrically defined EGJ outflow obstruction, EUS can evaluate for pseudoachalasia or external compression from adjacent structures which may mimic achalasia, although this is infrequently encountered [79].

Emerging Technologies: Functional Luminal Imaging Probe (FLIP)

The functional luminal imaging probe (FLIP) is an FDA-approved device (EndoFLIP, Crospon, Galway, Ireland) which can simultaneously obtain pressure and luminal diameter measurements within the gastrointestinal tract (Fig. 4.8). It is gaining clinical trial data primarily in disorders of the esophagogastric junction, such as achalasia. Applications in the evaluation of esophageal dysmotility and eosinophilic esophagitis are also emerging [80–83]. Commercially available since 2009, the FLIP catheter is positioned across the EGJ, and utilizes high-resolution impedance planimetry sensors housed within a volume-controlled distensible balloon which allows cross-sectional area to be measured. A solid-state pressure transducer is also housed within the apparatus which allows for simultaneous pressure measurements as well as distensibility of the lumen and most notably, the EG junction. Software analysis allows for determination of a distensibility index (DI) which provides complementary diagnostic value preoperatively to high-resolution esophageal manometry, and may have predictive value both intraoperatively and postoperatively as a measure of the effectiveness of myotomy [84–87].

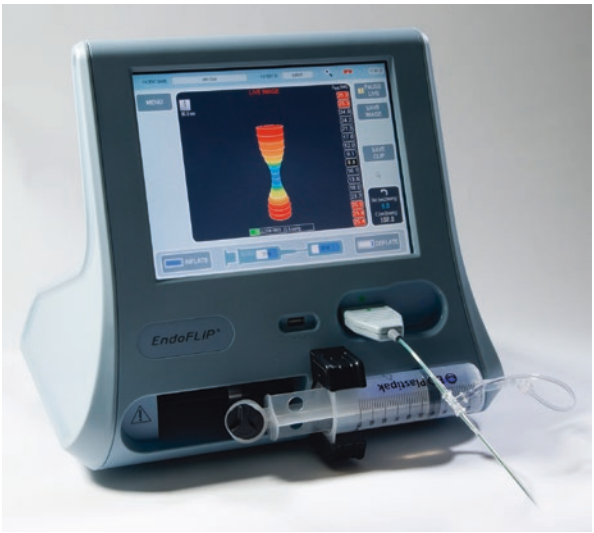

Fig. 4.8 EndoFLIP system (EF-100) with three-dimensional image of the EGJ. (Image courtesy of Crospon, Galway, Ireland)

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