Gastrointestinal Motility, Part 1: Esophageal Transit and Gastric Emptying

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Although not as well standardized as gastric emptying (GE) scintigraphy, esophageal transit scintigraphy, if performed in a comprehensive manner including both quantitative and qualitative analysis of single- and multiple-swallow studies, is clinically useful when expertise in esophageal manometry is not available or not tolerated and when esophageal manometry or barium videofluoroscopy results are equivocal or nondiagnostic. GE scintigraphy has undergone much-needed standardization. Both solid and liquid GE studies play an important role in assessing patients with upper gastrointestinal symptoms. Because measurement of simple total GE is often not sufficient to explain patient symptoms, there is a need to expand the analysis of GE scintigraphy to include the separate roles of the fundus and antrum and to include the complex interactions the stomach has with other organ systems.

Key Words: gastrointestinal scintigraphy; esophageal transit scintigraphy; gastric emptying scintigraphy

Motility studies performed by gastroenterologists typically require placement of a tube or catheter-based probe within the gastrointestinal tract to measure pressure, electrical signal, or pH. More recently a less invasive technique, wireless capsules, has been introduced (*1*). The advantages of scintigraphy for studying gastrointestinal motility have remained the same since the first description of a radiolabeled meal to measure gastric emptying (GE) (*2*). In contrast to probe methods, scintigraphy is noninvasive, does not disturb normal physiology, and accurately quantifies the bulk transit of a radiolabeled solid or liquid meal throughout the gastrointestinal tract. Compared with radiographic methods, scintigraphy involves low radiation exposure, is quantifiable, and uses commonly ingested foods rather than barium or radiopaque markers. Part 1 of this continuing medical education review addresses gastrointestinal scintigraphy as it applies to motility studies of the esophagus and stomach. Part 2 will address applications in the small bowel and colon.

CLINICAL INDICATIONS

Gastroenterologists are faced with a wide range of symptoms in their patients: pain, nausea, vomiting, bloating, diarrhea, constipation, or difficulty passing feces. Symptoms often overlap, and there are often questions about whether the symptoms are due to a structural or tissue abnormality or are functional (*3*). Symptoms may be associated with meal ingestion or may be unrelated to meals. A detailed Rome classification system has been developed to better classify functional gastrointestinal disorders when symptoms cannot be explained by an organic cause (*4*). Table 1 summarizes the symptoms for which gastroenterologists, in an attempt to seek an explanation, may order a gastrointestinal motility study.

GENERAL METHODOLOGY

A planar γ camera is typically used for imaging studies of gastrointestinal tract motility. The preference is to use the entire large field of view of modern cameras so that the region from the mouth to the stomach is included for esophageal transit studies and the entire abdomen is included for gastroenterocolonic studies. For dual-isotope studies of mixed solids and liquids, a medium-energy collimator is used to image the energies of ^{111}In (172 and 247 keV) and ^{99m}Tc (140 keV). A low-energy collimator is adequate for single-isotope ^{99m}Tc studies.

The most commonly used radioisotopes for gastrointestinal transit studies are ^{99m}Tc and ^{111}In. The final form in which the radioisotope is administered depends on the study to be performed. For studies of upper gastrointestinal transit, ^{99m}Tc

TABLE 1
Rome III Classification of Functional Gastrointestinal Disorders

Adult	Infant	Child/adolescent
A: Esophageal	G1: Infant regurgitation	H1: Vomiting and aerophagia
A1: Heartburn	G2: Infant rumination	H1a: Rumination
A2: Chest pain	G3: Cyclic vomiting	H1b: Cyclic vomiting
A3: Dysphagia	G4: Infant colic	H1c: Aerophagia
A4: Globus	G5: Functional diarrhea	H2: Abdominal pain
B: Gastroduodenal	G6: Infant dyschezia	H2a: Dyspepsia
B1: Dyspepsia	G7: Functional constipation	H2b: Irritable bowel
B2: Belching		H2c: Abdominal migraine
B3: Nausea/vomiting		H2d: Childhood abdominal pain
B4: Rumination		H3: Constipation and incontinence
C: Bowel		H3a: Functional constipation
C1: Irritable bowel		H3b: Nonretentive fecal incontinence
C2: Bloating		
C3: Constipation		
C4: Diarrhea		
C5: Unspecified		
D: Functional abdominal pain		
E: Biliary		
F: Anorectal		

is usually administered orally as ^{99m}Tc-sulfur colloid. ^{99m}Tc-sulfur colloid has a short half-life of 6 h and when properly cooked is physically bound to certain foods. Because it cannot be absorbed within the gastrointestinal tract, it causes only low radiation exposure (5). With a longer half-life of 67 h, ^{111}In-diethylenetriaminepentaacetic acid can be used to image gastrointestinal transit that requires 2–3 d, such as colonic transit. It usually is given orally, suspended in liquid, and also is nonabsorbable. ^{67}Ga complexes have also been used for gastrointestinal transit studies that extend over several days (6).

Before 2007, there were no consensus guidelines on standardized scintigraphic gastrointestinal transit studies. Thus, there was a lack of consistency in performing and reporting these studies (7,8). Recent guidelines on both GE (9) and small-bowel and colonic transit studies (10) now provide guidance on the technical details of performing and interpreting these studies. In this review, the reader will be referred to these guidelines for many of these details. This review will emphasize the physiologic and clinical knowledge needed for their proper interpretation.

ESOPHAGEAL TRANSIT

The decision on which diagnostic study to use for esophageal dysmotility depends on the symptoms. If dysphagia is present, a barium swallow or endoscopy is usually performed first to exclude an anatomic lesion. If these anatomic studies are not diagnostic, manometry will likely be performed to look for esophageal dysmotility. Manometry is considered the gold standard for diagnosis of the primary esophageal motility disorders, which include achalasia, scleroderma, diffuse esophageal spasm, hypertensive lower esophageal sphincter, and nonspecific esophageal motility disorders. Manometry, however, has limitations; it provides only an indirect measure of

peristalsis, as the pressure waves recorded do not always correlate with the aboral forces applied to a solid or liquid bolus in the esophagus. In addition, the presence of a manometric tube itself may affect normal physiology, and quantification of the volume of retained solids or liquids in the esophagus is not possible.

Early scintigraphy studies of esophageal transit demonstrated a high sensitivity for detecting a wide range of esophageal disorders (11,12) but a lower sensitivity, especially for disorders with intact peristalsis but high-amplitude contractions or isolated elevated pressures in the lower esophageal sphincter (13).

Currently, use of esophageal transit scintigraphy is limited despite its validation, in part due to the lack of a single, standardized method for performing the test. In comparison to GE and bowel transit studies, no consensus guideline has been established for esophageal transit scintigraphy. In addition, esophageal manometry as performed by gastroenterologists has matured from a research tool to a more clinically available and standardized test, thus further limiting the use of esophageal transit scintigraphy (14).

The simplest measure of esophageal transit is the time required for a liquid bolus of 15–30 mL of water containing 3.7–11 MBq (0.1–0.3 mCi) of either ^{99m}Tc-diethylenetriaminepentaacetic acid or ^{99m}Tc-sulfur colloid to transit the esophagus after a single swallow. Dynamic images after a swallow are typically recorded at a rapid rate of 0.25–0.5 s per frame for up to 30 s to capture both regional and total esophageal transit. Either single anterior or single posterior views of the chest have been used for esophageal transit scintigraphy.

Quantitative regional and total esophageal transit is usually analyzed by considering the total esophagus and its upper, middle, and lower thirds. Time–activity curves are generated for transit of the bolus through these regions. Esophageal
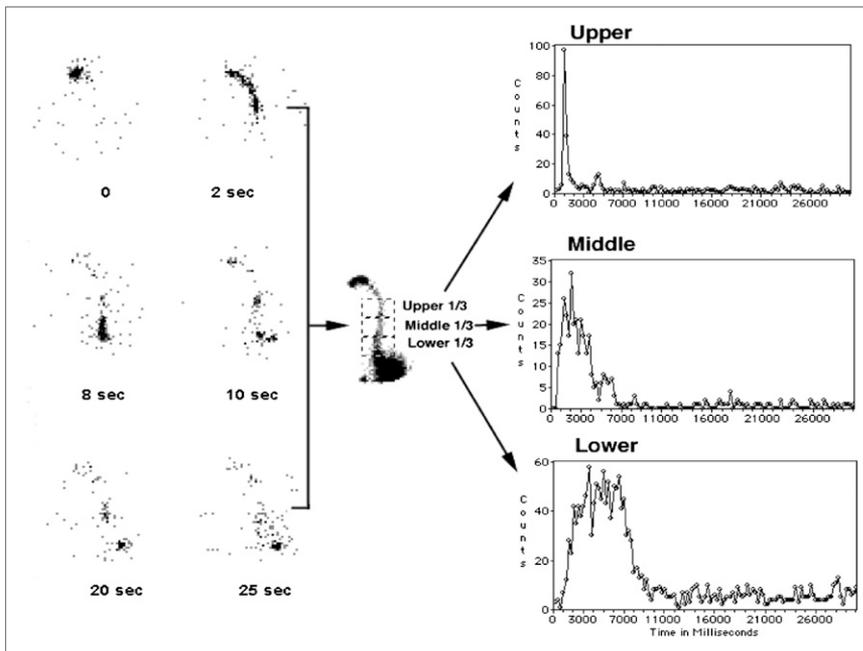
FIGURE 1. Normal esophageal transit (single swallow). Sequential dynamic images (left, 0–25 s) demonstrate normal bolus transit through esophagus. Composite image (center) is produced by summing all images from the initial 30 s. Regions of interest (dotted lines) that define upper, middle, and lower thirds of esophagus are shown. Time–activity curves (right) show counts recorded in each region as bolus progresses down esophagus. Esophageal transit time (11 s) is measured from time–activity curves of leading to trailing edges of upper and lower thirds of esophagus.

transit time is reproducible, with a reference range of 6–15 s (*13,15*). The resulting regional transit curves appear similar to manometric tracings (Fig. 1). A composite image summarizing all the regional transit data into one image may also be used (*16*). Review of the static condensed image is advantageous, but careful review of a dynamic (cine) display is also important, especially to observe tertiary contractions or subtle gastroesophageal reflux.

In addition to analyzing bolus transit after a single swallow, the percentage of total counts remaining in the esophagus after a single or multiple dry swallows is used to quantify total esophageal emptying. Some practitioners measure the decrease in the percentage of esophageal activity at 10 s after peak (normal, >83%) (*17*). Others have the patient perform serial dry swallows every 30 s for 10 min, with images acquired for 30 s each (*11*). A

region of interest comprising the entire esophagus is manually defined for this analysis (Fig. 2).

The counts in the esophagus (E_t) are plotted as a percentage of maximal counts in the total esophageal region of interest (E_{max}):

$$\% \text{ esophageal counts} = E_{max} - E_t/E_{max}.$$

Normally, more than 82% of the esophagus empties after 10 min of serial dry swallows (Table 2). Using the 10-min multiple-swallow method, the primary esophageal motility disorders demonstrate characteristic esophageal emptying patterns (Fig. 3). Like the single-swallow dynamic image series, the multiple-swallow series should be reviewed both quantitatively and qualitatively using cinematic computer display to detect any episodes of gastroesophageal reflux.
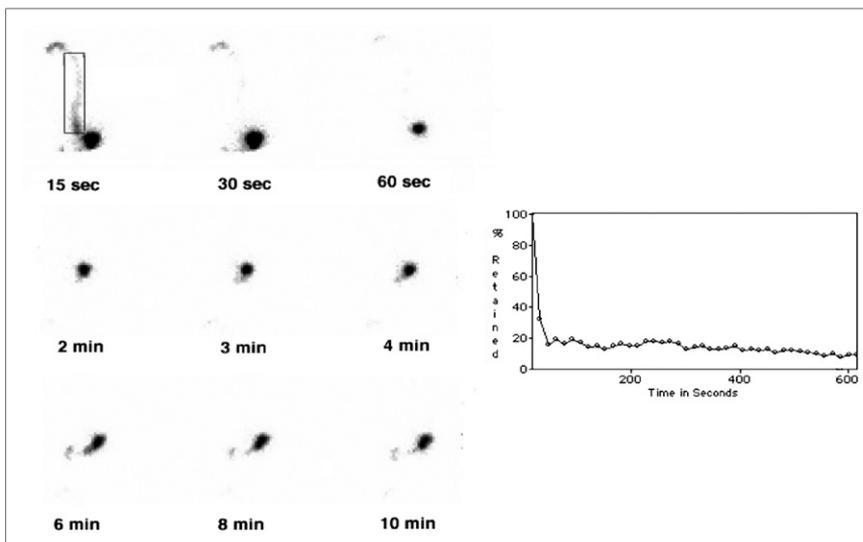

FIGURE 2. Normal global esophageal emptying (multiple swallows). Sequential images at 15 s per image are shown (left). Region of interest (rectangular box) is drawn over entire esophagus. From this region, time–activity curve (right) is generated showing percentage of activity retained in esophagus at each time. Amount of activity retained after multiple swallows can be used to help characterize primary esophageal motor disorders (Fig. 3; Table 1) or to follow therapeutic interventions as in achalasia.

TABLE 2
Diagnostic Criteria for Esophageal Transit Scintigraphy (11)

Condition	Visual bolus transit analysis from dynamic display	Esophageal transit time	Esophageal retention at 10 min
Normal	Normal aboral bolus transit through upper, middle, and lower thirds of esophagus with normal relaxation of lower esophageal sphincter	<14 s	<18%
Nonspecific esophageal motility disorder	Any localized abnormal retrograde–antegrade bolus movement (normal movement is mild, transient, and retrograde in distal esophagus before relaxation of lower esophageal sphincter, which clears rapidly)	>14 s	>18%
Isolated lower esophageal sphincter dysfunction	Normal bolus transit in upper and middle esophagus with delayed transit localized at gastroesophageal junction	>14 s	Usually <18%; may see mild retention of <30%
Scleroderma	Marked delay in bolus transit, typically localized to distal esophagus	>30 s	>30%, with marked improvement when upright
Diffuse esophageal spasm	Repetitive retrograde–antegrade contractions throughout esophagus	>14 s	Normal or mild retention, <30%
Achalasia	Marked delay in bolus transit throughout esophagus (may progress normally in upper esophagus from oropharyngeal propulsion)	>30 s	>50%, with no improvement when upright

Barium swallow studies have shown that as many as 5 swallows may be needed to maximize sensitivity for detecting an abnormal swallow. Use of up to 6 swallows has also been proposed to optimize esophageal transit scintigraphy (18). Esophageal transit scintigraphy using both supine and erect swallows together with a single swallow and total esophageal emptying has been compared with manometry and videoesophagography and found to have similar sensitivity for detecting primary as well as nonspecific esophageal motility disorders (11). On the basis of these results, specific criteria for diagnosing the primary esophageal motility disorders have been proposed (Table 2).

A nonspecific esophageal motility disorder is characterized by one or more minor manometric abnormalities. There have been conflicting results on the sensitivity of esophageal transit scintigraphy for nonspecific esophageal motility disorders, with some studies showing low sensitivity (42%–56%) (19). Use of a more viscous or semisolid bolus (gelatin) has been suggested to increase sensitivity.

Although the clinical role of esophageal transit scintigraphy has been limited, it is particularly useful when esophageal manometry is not available or not tolerated by the patient and when esophageal manometry results are equivocal or nondiagnostic. The ability of esophageal transit scintigraphy to quantitate total esophageal emptying is useful for assessing response to therapy in achalasia. Esophageal transit scintigraphy and barium videofluoroscopy should be considered complementary for achalasia, as optimal sensitivity for detecting esophageal dysmotility is achieved when both are used (20).

GASTRIC EMPTYING

GE studies are usually ordered to confirm or exclude whether gastroparesis (delayed GE) is a cause of a patient's symptoms. Gastroparesis is usually associated with upper gastrointestinal symptoms, which include nausea (92% of patients), vomiting (84%), abdominal fullness or distention (75%), or early satiety (60%) (21). Etiologies for gastroparesis include diabetes; infections; neuromuscular, autoimmune, and connective tissue diseases; cancer; and postsurgical effects or may be idiopathic. Diabetic gastroparesis is usually associated with retinopathy, neuropathy, and nephropathy (9).

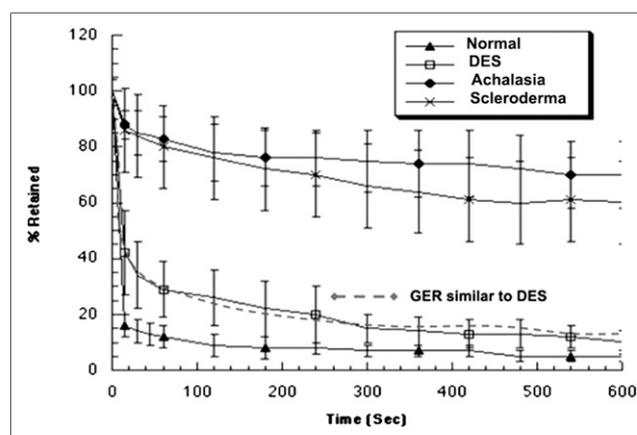Patients often do not have well-defined gastrointestinal symptoms and present with complaints of dyspepsia (symptoms

FIGURE 3. Esophageal emptying for primary esophageal motility disorders. Mean data for healthy subjects are shown compared with diffuse esophageal spasm (DES), achalasia, and scleroderma. Emptying curve for patients with esophagitis from gastroesophageal reflux is similar to DES. (Adapted from (75).)
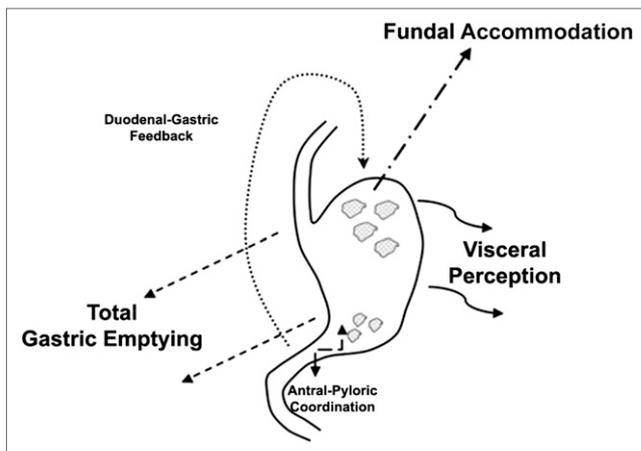
FIGURE 4. Multiple factors associated with GE are considered important to explain dyspeptic patient symptoms. Total GE, impaired fundal accommodation, and visceral hypersensitivity are 3 major factors currently under study. Antral–duodenal coordination and duodenal–gastric feedback mechanisms are also considered important but are not as well characterized. (Modified from (*76*).)

thought to originate in the upper gastrointestinal tract). Dyspepsia can be defined as any pain or discomfort in the upper abdomen. In 50% of patients with dyspepsia, no cause is found and the dyspepsia is classified as either idiopathic, essential, nonulcerous or functional dyspepsia (FD) (*22*). The Rome III classification of dyspepsia associated with gastroduodenal symptoms (Table 1) can further be classified as postprandial fullness, early satiation, epigastric pain, or epigastric burning (*23*). The goal of diagnosing delayed GE is to identify patients who will benefit from either a prokinetic drug or other treatment to alleviate symptoms. A GE study is indicated for patients with suspected gastroparesis or dyspepsia only after an anatomic cause for symptoms has been excluded. A GE study may also be indicated in the absence of gastric symptoms in some patients: those with severe gastroesophageal reflux disease not responding to acid suppressants, to see if delayed GE contributes to reflux; those requiring a work-up to identify a diffuse gastrointestinal motility disorder; and those who are diabetic and have poor glycemic control.

GE scintigraphy performed with a radiolabeled meal has remained the gold standard based on the fact that once the meal is radiolabeled, the counts measured by the γ camera are directly proportional to the volume of meal in the stomach independent of any geometric assumptions. As currently performed in most centers, GE scintigraphy is limited to measurement of either a delay or an acceleration in the emptying of a solid radiolabeled meal. Numerous studies, however, have shown a weak correlation between patients' symptoms and the results of measuring only total GE. Several studies, including a single large metaanalysis of 17 studies totaling 868 patients, found only up to a 40% incidence of delayed GE in symptomatic patients (*24,25*).

Because of the weak correlation between measurement of GE and symptoms, more recent studies have sought to determine whether there is a relationship between symptoms and other factors (not just total GE) that can be evaluated during GE scintigraphy (Fig. 4). Postprandial pain, belching, and weight loss have been associated with visceral hypersensitivity to gastric distension (*26*). Impaired fundal accommodation has been associated with early satiety (*27*), and fullness has been associated with late fundal retention (*28*). The rate of gastric emptying is affected by feedback mechanisms that coordinate antral contractions with pyloric relaxation. Nutrient receptors (glucose and osmolar) in the duodenum further control the rate of nutrient flow into the proximal small bowel (*29*).

In interpreting GE studies, one therefore needs to understand the multiple factors that affect GE, particularly the separate roles of the fundus and antrum. Visual inspection of early distribution of a solid meal in the stomach has become increasingly recognized as important. Although liquids rapidly disperse throughout the stomach, solids normally will initially localize predominantly in the fundus until slow, sustained fundal contractions move them to the antrum. This early localization of solids preferentially in the fundus (accommodation response) is visually apparent in the initial images of a solid-meal GE study (Fig. 5). A persistent transverse band separating the fundus from the antrum may be observed.

Measured counts increase as solids move from the posteriorly located fundus down into the more anteriorly located antrum, closer to the γ camera when positioned in front of the patient. Depth-related attenuation correction is performed using the geometric mean: (anterior counts × posterior counts)$^{1/2}$. This correction results in only a 3%–4% error in counts for the depths typically encountered (*30*). Collection of geometric mean data using anterior and posterior views does not require a dual-head camera system. Because gastric counts will not change significantly within 1 min, a single-head camera can be used by simply having the patient first face the camera and then face away from the camera, with a 1-min gastric image obtained each time. If the patient is unable to stand for anterior and posterior views, a single left anterior oblique view can be used for attenuation correction (*31*).

After the solids have moved into the antrum, peristaltic contractions work by a process called trituration to mix and break down the large solids into small particles in the presence of gastric digestive fluids. The solids must be reduced into particles of 1–2 mm before they will pass through the pylorus. The contractile activity of the antrum is controlled by a pacemaker located high on the greater curvature at the boundary between the fundus and the antrum. The time required to complete trituration so that solid particles are small enough to empty from the stomach has been referred to as the lag phase. Once triturated, the small, solid particles are suspended in the liquid within the stomach; they then empty monoexponentially at the same rate as the liquids (*32*).

Emptying of liquids is controlled by a sustained pressure gradient generated by the fundus. Liquids require no trituration, and they empty monoexponentially (Fig. 5) and more rapidly than solids, with no lag phase. A previously held belief
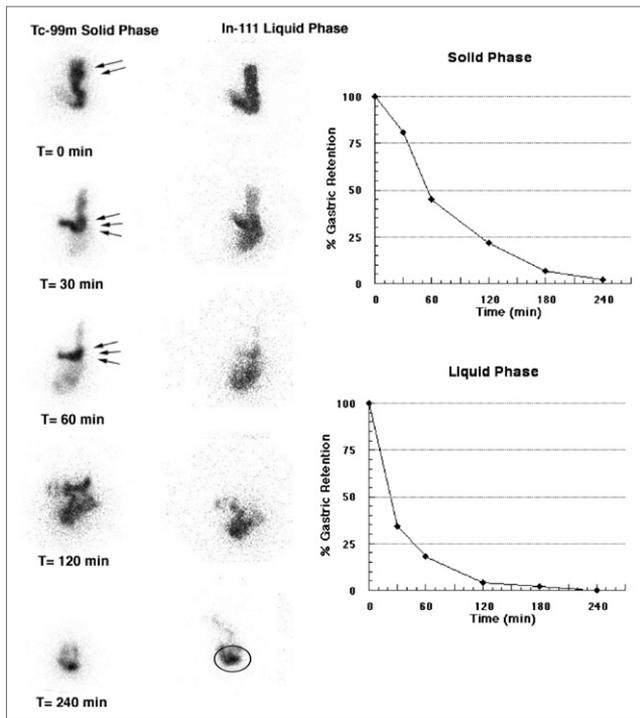
FIGURE 5. Normal dual-isotope, solid–liquid GE study (anterior views only). These images demonstrate early rapid distribution of liquids throughout stomach at 0 min. Liquid emptying curve is monoexponential. In contrast, solids show preferential early fundal localization (accommodation) (double arrows). Over time, solids progress down into antrum (triple arrows). Solid emptying curve is sigmoidal because of early lag phase for solids. Over time, one can observe small-bowel transit of solids and liquids, with buildup of activity in the terminal ileum (oval region of interest).

was that liquid GE added little to the evaluation of patients with dyspepsia (33,34). It was felt that since the liquids require no trituration, liquid GE remained normal until gastroparesis was at an advanced stage and that liquids were therefore less sensitive than solids for detecting early gastroparesis (35). One early study found delayed liquid emptying but normal solid emptying in 24% of diabetic patients (36).

Recently, there has been increased interest in the role of liquid GE studies to supplement solid-meal GE studies. An association has been reported between delayed GE of solids and liquids and symptoms of postprandial fullness, nausea, and vomiting. Multivariate analysis has shown that postprandial fullness and early satiety are associated with delayed liquid GE (37). Liquid GE studies have also been used clinically because rapid emptying of nutrient-containing liquids may be associated with early satiety, nausea, or vomiting in the dumping syndrome (34).

In combined dual-isotope solid- and liquid-phase meals (^{99m}Tc-labeled egg and ^{111}In-diethylenetriaminepentaacetic acid in water), liquid GE may appear abnormal when solid GE is normal. One study of 476 patients found only a 5% incidence of delayed liquid GE when solid GE was normal (35). Another study, however, found that 26% of patients (57

nondiabetic) had normal solid GE but delayed liquid GE (38). Abnormal GE of solids was mildly correlated with nausea, vomiting, loss of appetite, early satiety, and a feeling of excessive fullness after meals. Liquid GE was associated more with early satiety and loss of appetite.

Ziessman et al. reported on a combined retrospective and prospective study in which a nonnutrient, liquid GE study was performed independently of a solid meal (39). The liquid meal consisted of 500 mL of tap water mixed with ^{99m}Tc-sulfur colloid. The solid and liquid GE studies were performed on separate days retrospectively and then sequentially (liquid meal for 30 min followed by solid meal for 4 h in a prospective study). In the retrospective study, 17 of 21 patients had normal solid GE. Of these, 13 (76%) had delayed liquid GE. In the prospective study, 10 patients (33%) with normal solid GE had delayed liquid GE. In a second larger study of 101 patients who underwent both solid- and liquid-meal GE on the same day with the same protocol, delayed GE was found in 36% of liquid studies and 16% of solid studies. Of patients with normal solid emptying, 32% had delayed liquid emptying. On the basis of these results, these authors suggested that a nonnutrient, liquid GE study may detect fundal gastric dysmotility and help to improve the detection rate of gastric dysmotility in patients with FD (40).

These recent studies further suggest a role for liquid GE studies, but the physiologic effects of a nonnutrient, liquid meal have not been well studied in patients with FD. When given after a nutrient meal, a water load has been shown to inhibit antral motility and increase cholecystokinin release in healthy subjects. It is theorized that an increase of cholecystokinin is a response to inflow of fatty chyme into the duodenum, with the resultant feedback slowing entry of the meal into the duodenum. This duodenogastric interaction has been termed the duodenal break (41). Further studies of the physiology and clinical significance of use of a nonnutrient, water–liquid meal is needed.

Until recently, there were no accepted standards for performing GE scintigraphy. This problem raised concerns about the continued acceptance of GE scintigraphy without consistent methodology (8). As a result, in 2007 a consensus recommendation was published jointly by the Gastrointestinal Council of the Society of Nuclear Medicine and Molecular Imaging and the American Neurogastroenterology and Motility Society (9). The consensus group recommended a solid-meal GE test "using readily available technology and normative data, which can provide clinicians with standardized results." This consensus recommendation was adopted by the Society of Nuclear Medicine and Molecular Imaging (42) and was included in a joint practice guideline from the American College of Radiology/Society for Pediatric Radiology and the Society of Nuclear Medicine and Molecular Imaging (http://www.acr.org/~/media/ACR/Documents/PGTS/guidelines/GI_Scintigraphy.pdf).

Normal values were established not only for the meal but also for the method of acquiring and processing the images. GE was also standardized for body position, smoking, phase

of the menstrual cycle, and time of day the test is performed (43–45). Medications such as prokinetic agents, antisecretory drugs, gastric acid suppressors, and narcotics affect GE. Patients are instructed to fast overnight and to stop any medications that might affect GE. Prokinetic drugs that can accelerate GE, such as metoclopramide (Reglan; Baxter Pharmaceutical), tegaserod (Zelnorm; Novartis), erythromycin, and domperidone (Motilium; Janssen Pharmaceutica), are stopped at least 2 d before the test. Drugs that can delay GE are also stopped for 2 d before the test, such as the opiates meperidine (Demerol; Sanofi-Aventis), codeine, morphine, and oxycodone (OxyContin; Purdue Pharma) and the anticholinergic antispasmodic agents dicyclomine (Bentyl; Aptalis Pharma US), belladonna, phenobarbital (Donnatal; Rebel Distributors Corp.), hyoscyamine (Levsin; Alaven Pharmaceutical), and glycopyrrolate (Robinul; Baxter Healthcare). Patients may take other medications with a small quantity of water the morning of the test. Smoking is prohibited starting the morning of the test and during the 4 h of imaging.

The importance of glucose control in diabetic patients is emphasized. Diabetic patients should have their fasting glucose level checked before the test begins. If the glucose level is 275 mg/dL or higher, a small dose of short-acting insulin may be administered before meal ingestion and the patient then monitored until the level falls below 275 mg/dL. Diabetic patients should be instructed to bring their insulin with them, and if their glucose level is under 275 mg/dL, told to take approximately half their standard daily dose of insulin upon ingestion of the test meal because they will not eat during the next 4 h.

The consensus group recommended use of a low-fat meal based on normative data from a large multicenter study (46). The meal comprises 120 g (4 oz) of Eggbeaters (ConAgra Foods) or a generic liquid egg-white equivalent, mixed with 18.5–37.0 MBq (0.5–1.0 mCi) of ^{99m}Tc-sulfur colloid, 2 slices of white bread, 30 g of strawberry jam, and 120 mL of water. The total energy of the meal is 255 kcal (72% carbohydrate, 24% protein, 2% fat, and 2% fiber). ^{99m}Tc-sulfur colloid binds to the egg white during cooking. A recent study has shown that the liquid egg white can be cooked using either a skillet or a microwave, provided it is cooked to a firm consistency (47).

The patient is instructed to consume the meal within 10 min. Immediately after eating the meal, the patient is imaged while standing or, if necessary, supine. Supine positioning throughout the study should be avoided as it can significantly slow GE of solids (48). The recommended time points for obtaining GE scintigraphy images are at 0, 60, 120, 180, and 240 min after meal ingestion. An image at 30 min may be helpful if rapid GE or impaired fundal accommodation is suspected. Regions of interest corresponding to the stomach are typically manually defined to analyze the total gastric counts. Decay- and depth (attenuation)-corrected total gastric counts are calculated for each time point. The percentage of activity remaining in the stomach normalized to 100% for maximal gastric counts is reported.

When the consensus-recommended solid meal is used, GE is considered delayed if gastric retention is more than 60% at 2 h or more than 10% at 4 h. Because the symptoms of rapid GE can mimic those of delayed GE, the consensus also defines values for rapid GE as being retention of less than 70% at 30 min or less than 30% at 1 h.

Other ancillary methods have been used to analyze GE data (see below). These include the time to 50% emptying of the meal. It is recommended that GE scintigraphy be performed for up to 4 h, because studies have shown percentage gastric retention to have greater sensitivity for detecting abnormal GE (49) and to be most reproducible (50). If there is abnormal retention at 2 h, the study may be terminated because GE is already delayed. One group of investigators has published criteria for early termination at 2 h. Although early termination could reduce the total time of imaging for some patients, there was a small loss of sensitivity (51).

Because of the individual roles of the fundus and antrum, some patients may show abnormal GE at 2 h and normal GE at 4 h. In others, GE may be normal at 2 h and abnormal at 4 h. This result is not unexpected because the early phase (0–2 h) of a solid GE study reflects primarily fundal function and the later phase (2–4 h) reflects primarily antral trituration and propulsion of the meal into the duodenum. Future therapies may target the fundus and antrum differently.

The consensus GE group also made recommendations on important ancillary issues in the reporting of GE studies. All reports should include an estimate by the technologist of the total amount of meal ingested. Because the normal values for GE are based on ingestion of the entire standard meal, if only a small portion of the meal is ingested the study cannot be considered diagnostic. If the patient has not ingested the full meal, the report should state that the results may overestimate the rate of GE. The GE report should also state whether any incidental abnormal findings were observed, including esophageal retention or reflux of the meal, hiatal hernia, fundal wrap, or lack of fundal accommodation.

The consensus group recognized the complexity of GE and the limitations of their current recommendations. They acknowledged that numerous items will require further clarification, including optimization of image times, need for normative data on other substitute meals, the role of glycemic control in diabetic patients, the value of monitoring symptoms during the study, a scale to assess the severity of delayed GE, the need for normal postsurgical gastric reference data, the clinical role of analyzing fundal and antral gastric function, and other potential methods of quantitation (curve fitting, lag phase, total abdominal counts).

Delayed GE may be suspected in infants who have vomiting, abdominal pain, or early satiety. The consensus recommendations were developed only for adults. Unfortunately, no adequate standards have been developed for measuring GE in children. In infants, GE scintigraphy is usually performed with evaluation of gastroesophageal reflux. This study may be performed with the child's milk or formula to which ^{99m}Tc-sulfur colloid has been added. Adequate normal values for GE

in children after various meals have not been established. A range of gastric retention of 40%–70% at 1 h has been reported (*52*).

ANCILLARY TESTS OF GASTRIC FUNCTION

Delayed GE is found in a significant, but only limited (30%–70%), number of symptomatic patients with diabetes or functional dyspepsia (*53*). It is increasingly recognized that a more detailed study of GE beyond just total GE is needed to fully evaluate gastric function. Analysis of GE in the future will likely include attention to separate fundal and antral motor function, fundic relaxation (accommodation response), visceral hypersensitivity, asynchronous antroduodenal coordination, and gastric dysrhythmias (*37,54–55*). Other measures of gastric function that have been studied as a part of GE scintigraphy but currently are not routinely performed are described below.

Lag Phase Analysis

Numerous studies have confirmed the presence of an early lag (trituration) phase for solids followed by a phase during which the stomach empties solids at a characteristic rate (*56–58*). To completely characterize these phases of GE, it is best to fit the data to a mathematic function known as a modified power exponential (*32*), given by

$$y(t) = 1 - [1 - \exp(-kt)]^{\beta},$$

where $y(t)$ is the percentage of gastric activity remaining at time t; k is the slope of the exponential portion of the curve; and β is the y intercept. The lag phase $(\ln(\beta/k))$ corresponds to the time of peak activity in the antrum, which physically corresponds to maximal filling of the antrum just before the adequately triturated small, suspended, solid particles begin to empty at the same uniform rate (k) as liquids. Imaging at only 0, 1, 2, and 4 h does not permit adequate curve-fitting analysis. Lag-phase analysis requires earlier and more frequent time points. There are few data, however, to support routine clinical analysis of the lag phase. In a recent study, Bonta et al. found that the lag phase was not predictive of delayed GE (*51*).

Fundal Accommodation and Intragastric Distribution Studies

Fundal relaxation (accommodation) is an established physiologic response that allows intragastric volume to increase without increasing the intragastric pressure (*59*). Early satiety is the predominant symptom associated with a poor accommodation response. Studies show a correlation between dyspeptic symptoms and hypersensitivity to fundal distension and impaired fundal accommodation (*60,61*).

The gastric barostat test measures the volume to which a gastric balloon can inflate at a given pressure and measures fundal compliance. Patients with visceral hypersensitivity experience symptoms at low levels of distention. Although barostat testing is the best direct measurement of fundal accommodation, the test has been criticized as invasive (*62*). A less invasive water load test has also been used to study the correlation between impaired accommodation and dyspeptic symptoms. Both water loading and nutrient liquid meals can be used to assess accommodation and produce symptoms in approximately 50% of patients with FD (*63*).

SPECT gastric accommodation studies make use of the fact that the gastric mucosa accumulates ^{99m}Tc-pertechnetate after intravenous administration. Three-dimensional SPECT volumetric imaging of the outer wall of the stomach can then be performed. SPECT has been validated as a noninvasive method to measure gastric volume (*64,65*). It is also possible to simultaneously assess the relationship of liquid- or solid-meal emptying and gastric accommodation. Such studies have shown that the maximal change in gastric volume (mean, 185%) occurs immediately after meal ingestion and persists despite relatively rapid emptying of the meal (*66*). Direct comparison of gastric postprandial-to-fasting volume ratios between a balloon barostat and SPECT has shown SPECT to provide an accurate measurement of the accommodation response in healthy and postfundoplication patients (*63*).

The added clinical utility of SPECT measurements of accommodation response was demonstrated in a review of a large number of patients with dyspepsia. Among the 214 patients reviewed, gastric accommodation was impaired in 47% of patients with dyspepsia and 25% of patients with normal GE (*67*). A study comparing a water-drink load test with SPECT gastric volumes found that fasting gastric volumes were significantly higher in patients with FD than in controls. The patients with FD ingested significantly less water and had impaired filling of the distal stomach after the water load test. However, symptoms of bloating, pain, and fullness were determined more by the proximal than by the distal stomach volume (*68*).

Abnormal intragastric distribution patterns have also been associated with symptoms of dyspepsia. In a study using SPECT, early proximal GE was lower, and the half-time of emptying of the proximal stomach longer, when SPECT gastric accommodation was impaired (*69*). In another study of accommodation response, the stomach was simply divided into proximal and distal segments. Early satiety was associated with early distal redistribution of the meal, and fullness was associated with later proximal retention (*28*).

Because abnormal fundal accommodation can be observed on routine planar GE images, the recent consensus on GE recommends evaluating the images for the presence of an abnormal accommodation response (*9*). The normal fundal accommodation response is best observed in the first set of images after solid-meal ingestion (at the 0-min time point). Typically, most of the solid meal will be localized in the upper half of the stomach. A lack of normal fundal accommodation may be an additional important finding to explain patient symptoms especially when GE is normal (Fig. 6).

There have been conflicting reports that impaired fundal accommodation results in more rapid GE. Impaired gastric accommodation from surgical fundoplication, gastric banding, and balloon placement promotes displacement of solids into the distal stomach and may result in rapid GE. In a study of patients with FD and low gastric accommodation, 13% of
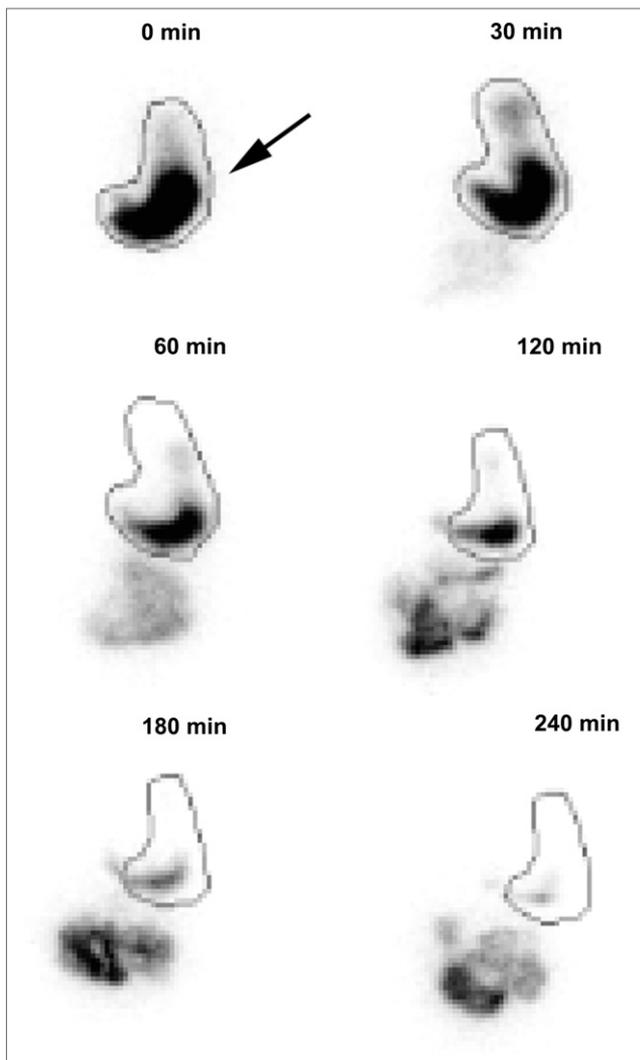
FIGURE 6. Impaired fundal accommodation (anterior views only). First postmeal ingestion image (0 min) shows lack of normal fundal accommodation, with most of meal being seen in distal stomach rather than in fundus (arrow). Overall GE was normal, with 42% of meal retained at 120 min and 8% at 240 min.

patients had rapid GE and 28% had normal GE (*67*). In contrast, Camilleri et al. found that proximal GE was reduced in patients with low postprandial accommodation but that overall GE in these patients was normal (*69*). They theorized that compensatory mechanisms accelerate overall GE despite delayed proximal GE.

Bicompartmental (Fundal–Antral) GE

Because scintigraphy easily permits analysis of the intragastric distribution of the test meal between the fundus and antrum, it is ideal for measuring both regional and total GE. Studies have shown an association between proximal gastric retention and symptoms of nausea, early satiety, abdominal distention, and acid reflux, whereas vomiting was associated more with delayed distal GE. Inspection of fundal and antral GE in the images and quantification of regional GE can be

helpful for explaining dyspeptic symptoms, especially when total GE is normal (*28,70*).

Antral Contraction Scintigraphy

Methods of measuring the frequency and amplitude of antral contractions have been developed. Antral contractions normally occur at a rate of 3 per minute. The ability to measure both the frequency and the strength of antral contractions has increased our understanding of normal and abnormal GE. In diabetic gastroparesis, GE is delayed not only by food retention in the fundus but also by weakened antral contractions that occur at a higher frequency (*71*). Most patients with gastroparesis are women, at up to an 82% predominance in a large study (*72*). Differences in normal male and female GE have been shown to be due to the amplitude of antral contractions and not the frequency. When scintigraphy was used to measure the amplitude of antral contractions, women were shown to have lower amplitude contractions not associated with the phase of the menstrual cycle (*73*).

PET Neuroactivation

Although not associated with conventional GE imaging, a future role for PET brain imaging to assess the brain–gut axis and its relationship to gastric function may gain importance in understanding patients with dyspepsia. PET of the brain has demonstrated specific neuroactivation pathways linked to fundal distention and symptoms of dyspepsia (*74*).

CONCLUSION

Although not as well standardized as GE scintigraphy, esophageal transit scintigraphy, if performed in a comprehensive manner including both quantitative and qualitative analysis of single- and multiple-swallow studies, is clinically useful when expertise in esophageal manometry is not available or not tolerated and when esophageal manometry or barium videofluoroscopy results are equivocal or non-diagnostic. GE scintigraphy has undergone much-needed standardization. Both solid and liquid GE studies play an important role in assessing patients with upper gastrointestinal symptoms. Because measurement of simple total GE is often not sufficient to explain patient symptoms, there is a need to expand the analysis of GE scintigraphy to include the separate roles of the fundus and antrum and to include the complex interactions the stomach has with other organ systems.

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Gastrointestinal Motility, Part 1: Esophageal Transit and Gastric Emptying

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