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Update on Gastrointestinal Scintigraphy

Alan H. Maurer, MD*, and Henry P. Parkman, MD†

Nuclear medicine offers a variety of studies for evaluating motility throughout the gastrointestinal tract. Gastric emptying remains the "gold standard" for studying gastric motor function, but its application in most centers remains limited to measuring only total gastric emptying in spite of data that show assessment of both fundal and antal function is of clinical value for evaluating patients with dyspepsia. Similarly, newer methods to study small bowel and colon transit have not gained widespread use. This review summarizes the state-of-the-art of prior established and newer scintigraphic studies with an emphasis on their clinical applications.
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It is now 10 years since our last review of gastrointestinal (GI) scintigraphy in *Seminars in Nuclear Medicine*. At that time, we editorialized that although the accuracy and ease of quantification of radiolabeled solids and liquids had made scintigraphy the gold standard for testing gastric emptying (GE), there were ongoing challenges from other modalities that could depose this gold standard.[1] Today, in most institutions, a GE study still usually is the only scintigraphic study used to evaluate patients with dyspepsia and suspected GI motor dysfunction. Despite research that has expanded our clinical tools, the technical advances developed during the last 10 years have not gained widespread clinical acceptance. GE studies usually are only evaluated for simple $T_{1/2}$ measurements or the percentage of the meal remaining at fixed times. There is little consistency on how GE studies are performed or the meal and normal values to be used to assess GE. Few imaging departments analyze separately proximal and distal gastric motor function. Small bowel and colon transit studies are limited to a handful of institutions.

Although the routine clinical application of scintigraphy for evaluating GI motility has been relatively static, our understanding of the complexity of evaluating and treating patients with GI dysmotility has expanded. Functional dyspepsia is a common presenting complaint for many patients and is estimated to affect 20% of the population of the United States.[2] The symptom complex typically is characterized by postprandial upper-abdominal discomfort or pain, early satiety, nausea, vomiting, abdominal distension, bloating, and anorexia in the absence of any previously documented organic cause. Patients with dyspepsia often are classified into subgroups based on the predominant symptom, ie, reflux-like, ulcer-like, or dysmotility, because treatment is guided by the patient's symptom. Gastric acid secretion inhibitors are recommended for ulcer-like dyspepsia and prokinetics for dysmotility-like dyspepsia.

Previous efforts to explain dyspepsia emphasized motility and sensory dysfunction of the stomach as primary mechanisms contributing to patient symptoms. Increasingly multiple factors, including motor abnormalities, gastric accommodation, altered visceral sensitivity, and psychosocial factors have all been recognized as central to this disorder. The role of functional imaging such as a GE study has played an important, but limited, role in the evaluation of patients because delayed GE (gastroparesis) occurs only in 30% to 60% of patients with functional dyspepsia and does not correlate well with symptoms.[3] Because symptoms associated with one part of the GI tract may overlap with another, recognition is increasing that GI transit studies of the stomach, small bowel, and colon are now an important part of the evaluation of patients with dyspepsia and constipation.[4]

The current challenge is to take this new knowledge and apply our more-advanced methods to better diagnosis and treat patients. In this update, we will review the current status of GI transit studies from the esophagus to the colon. We hope to briefly review the basics and highlight new studies such as those that assess both fundal and antral partitioning of the meal and measure gastric accommodation as well as antral contractility. In addition, more experience has been obtained with the combined use of GE, small bowel, and colon transit studies (whole-gut transit scintigraphy). Scintigraphy also will be compared with other new approaches that measure similar function using imaging and nonimaging methods.

*Nuclear Medicine, Temple University Hospital and School of Medicine, Philadelphia, PA.
†Gastroenterology Section, Temple University Hospital and School of Medicine, Philadelphia, PA.
Address reprint requests to Alan H. Maurer, MD, Nuclear Medicine, Temple University Hospital and School of Medicine, 3401 N Broad St, Philadelphia, PA 19140. E-mail: amaurer@temple.edu

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Table 1 Diagnostic Criteria for Radionuclide Esophageal Transit Scintigraphy (RETS)

Disorder	Visual bolus analysis from cine	Esophageal Transit Time (s)	Esophageal Retention at 10 min (%)
Normal	Normal antegrade bolus transit through upper, middle, and lower one-third esophagus with normal relaxation of the lower esophageal sphincter	<14	<18%
Nonspecific esophageal motility disorder	Any localized abnormal retrograde-antegrade bolus movement	>14	>18%
Isolated lower esophageal sphincter dysfunction	Normal bolus transit upper, middle esophagus with delayed transit localized at GE junction	>14	Usually <18%, may see mild retention >30%
Scleroderma	Marked delay in bolus transit, may be localized to distal esophagus	>30	>30% with marked improvement in upright position vs. supine
Diffuse esophageal spasm	Repetitive retrograde/antegrade contractions throughout the esophagus	>14	Normal or mild retention, <30%
Achalasia	Marked delay in bolus transit throughout esophagus, may progress normally in upper esophagus from oropharyngeal force	>30	>50%, no improvement in upright position

Modified from Parkman et al.[8]

Esophageal Transit

Which diagnostic study is used to evaluate a patient for esophageal dysmotility depends on the patient's symptoms. If dysphagia is present, a barium swallow, computed tomography (CT), or endoscopy usually is performed first to exclude an anatomic lesion. If anatomic studies are not diagnostic, manometry is then usually performed. In our experience, use of esophageal transit scintigraphy (ETS) is limited to when these other studies are nondiagnostic or when there is a need to quantitiate objectively the response to some therapy.[5]

ETS remains a noninvasive and quantitative method of assessing esophageal motility. It has been shown that as many as 50% of patients with dysphagia and normal manometry and barium studies demonstrate esophageal dysmotility with scintigraphy. Early studies reported a high sensitivity for detecting esophageal dysmotility, but later studies indicated lower sensitivity, especially for disorders with intact peristalsis but high-amplitude contractions or isolated elevation of lower esophageal sphincter pressures.[6,7] More recent studies confirm a high sensitivity for detecting a wide range of esophageal disorders.[8,9]

However, the widespread use of ETS is limited despite validation, in large part, because no single method for performing ETS has been standardized. The simplest measure of transit is the esophageal transit time (ETT), which is required for ^{99m}Tc-DTPA in water to transit the esophagus. ETT is reproducible with a normal range of 6 to 15 seconds.[7,10]

Dynamic images are recorded and then should be examined visually using computer display. Regional esophageal transit traditionally is analyzed by dividing the esophagus into upper, middle, and distal thirds. Time-activity curves can be generated for these regions of the esophagus. A condensed image that summarizes all the regional transit data into one image also may be used. Condensed images have the advantage of summarizing the data in a single image. However, proponents of the composite image acknowledge the importance of always reviewing the cine images as a movie.[11]

In addition to analyzing regional transit, the total counts remaining in the esophagus after multiple swallows should be obtained to quantify esophageal emptying. After the initial swallow, the subject performs dry swallows usually every 30 seconds for 10 minutes. An esophageal region of interest comprising the entire esophagus is defined for computer analysis and esophageal counts (E_t) are plotted as a percentage of maximal counts (E_{max}) such that the percentage of esophageal emptying $= E_{max} - E_t/E_{max.}$ Normally, no significant activity is found in the esophagus after 10 minutes.

There have been conflicting results on the sensitivity of ETS for nonspecific esophageal motility disorders, with some studies showing low sensitivity (42-56%).[12,13] Use of a more viscous, semisolid bolus or simply increasing the number of swallows performed can increase the sensitivity of ETS.[14] The use of multiple swallows (up to 6) has been proposed to optimize ETS.[15] Recently, ETS using supine and erect swallows was compared with manometry and videoesophagography and was found to have similar sensitivity for detecting the primary as well as nonspecific esophageal motor disorders. Using visual assessment of the cine of the liquid bolus transit combined with measurement of ETT and esophageal emptying, specific criteria for diagnosing primary esophageal motility disorders have been suggested (Table 1).[8] ETS and videofluoroscopy remain complementary, and optimal sensitivity for detecting esophageal dysmotility is achieved when both are used, especially for achalasia.[16]

Gastroesophageal Reflux (GER) and Pulmonary Aspiration

Adult Studies

GER scintigraphy was developed in adults to both detect and quantitate reflux. There have been no significant recent de-

velopments in the method to perform GER scintigraphy. Adults typically drink 300 μCi of ^{99m}Tc-SC suspended in 150 mL of orange juice mixed with 0.1 N of HCl. The patient is imaged supine under a gamma camera, and an abdominal binder is used to increase abdominal pressures in 20-mm increments up to 100 mm Hg. Computer images are recorded for 30 seconds at each level of binder pressure.

In normal individuals, no reflux is observed. When reflux occurs, activity can be visualized in the esophagus. Because abnormal esophageal transit and GER often are present in the same patient, it is best to perform both studies together. GER may be identified during review of the multiswallow esophageal emptying study, even when the abdominal binder pressure study is negative.[5]

Quantification of GER may be useful. The percentage value measured is given by: $R = E_p - E_b / G_o \times 100\%$, where R represents the GER index expressed as a percentage, E_p represents the esophageal counts at abdominal pressure p, E_b represents the background counts, and G_o represents the gastric counts at the beginning of the study. Early studies, which used a normal upper limit of 4%, reported reflux in 90% of patients with confirmed reflux and in only 10% of controls. The low counts (up to 4%) detected in normal patients is caused by "scatter" counts from the adjacent gastric fundus. Later studies have not consistently confirmed high sensitivity for detecting reflux.

GER scintigraphy has been shown to be complementary to 24-hour pH probe measurements to evaluate the volume of reflux, especially during rereflux episodes, which are underestimated by pH probe measurements.[17,18] GER scintigraphy appears to be most useful when there is a need to quantify the volume of reflux and changes in response to medical or surgical treatment. A GE study also is useful to evaluate patients with GER who may benefit from a prokinetic drug, as delayed GE is found in approximately 30% of patient using a 4-hour GE study.[19] An inverse relationship has been shown with decreased intragastric fundal retention of a liquid meal and increased episodes of GER.[20] Recent studies using ph probe measurements combined with GE also have confirmed a relationship of the amount of proximal extent of GER related to early postprandial fullness especially when ambulatory.[21] Attempts have been made to image pulmonary aspiration of gastric contents in adults. However, insufficient data exist to evaluate the role of scintigraphy for detecting aspiration in adults.

Pediatric Studies

In children, the "milk scan" is used to evaluate esophageal transit, GER, gastric emptying, and pulmonary aspiration. Previous studies, which compared scintigraphy with simultaneous pH probe monitoring, reported a sensitivity and specificity of 79% and 93%, respectively. In recent studies, scintigraphy found an incidence of reflux ranging from 20% to 40% in children from less that 1 year to 6 years of age.[22]

^{99m}Tc-SC usually is mixed with the child's usual volume of milk, formula, apple juice, or glucose water and is given at the time of a routine feeding. Images are recorded after the feeding is completed. Initial swallowing curves can be recorded to evaluate esophageal transit. With the patient lying supine on the camera, posterior images of the chest and abdomen are obtained for at least 60 minutes.[23] Visual cine review of computer-enhanced images increases sensitivity to detect small volumes of reflux. Time–activity curves are helpful to document the frequency of reflux, delayed esophageal clearance, and to improve reproducibility in the readings.[24] Rapid imaging (10-20 s/image) is important because transient reflux can rapidly dissipate. Delayed images at 1, 2, and 24 hours can be acquired to detect pulmonary aspiration. Pulmonary aspiration is documented with this method in 35% to 55% of children with severe pulmonary disease.[25]

Gastric Emptying

Patients referred for GE studies often do not have well-defined GI symptoms and present with complaints of dyspepsia (GI symptoms thought to originate in the upper GI tract). Gastroparesis is usually associated with upper-GI symptoms, including nausea (92%), vomiting (84%), distention (75%), or early satiety (60%).[26] In 50% of patients, no cause is found, and the dyspepsia is classified as idiopathic, essential, functional, or nonulcer dyspepsia.[27] An excellent review of the gastrointestinal and systemic diseases associated with gastroparesis has been published by the American Gastroenterological Association.[28]

A functional GE study is indicated for patients with dyspepsia after an anatomic cause has been excluded. A GE study also may be indicated in the absence of gastric symptoms for patients with severe GER disease not responding to acid suppressants, for identification of a pan motility GI disorder, or evaluating a diabetic with poor glycemic control.

Understanding the separate roles of the fundus and antrum has become increasingly important for analyzing GE studies. Normally solid foods are temporarily stored in the fundus until slow, sustained contractions transfer the solids to the antrum. Emptying of liquids is controlled by a sustained pressure gradient generated by the fundus. Liquids require no trituration and are distributed rapidly after ingestion throughout the stomach from the stomach monoexponentially. Liquid GE studies by themselves are of little clinical value because liquid emptying usually is not abnormal until gastroparesis is far advanced.[29] Solid-phase studies usually will reveal delayed GE earlier than liquids. Occasionally, a liquid only study is useful if a patient is unable to tolerate a solid meal. In such a case, if liquid emptying is abnormal, significant gastroparesis is usually present.

Normal values for a variety of meals, including meats, porridge, pancakes, eggs, and chemical resins, have been reported. For any test meal, the stability of the radioisotope bound to the solid phase must be established to ensure that the radioisotope does not dissociate in gastric juice. A large multicenter study has established normal values for a commercially available egg meal using 0.5 mCi of ^{99m}Tc-SC, 120 g of egg (EggBeaters; ConAgra Foods, Inc, Omaha, NE), 2 slices of white wheat bread, 30 g of strawberry jam, and 120 mL of water (255 kcal, 24% protein, 2% fat, 72% carbohy-

drate, 2% fiber).[30] The 1-hour, 2-hour, and 4-hour values for the percentage of the meal retained are very similar to a similar meal consisting of 2 large whole eggs, 2 pieces of white toast, and 300 mL of water (282 kcal, 22% fat, 32% protein, 46% carbohydrate).[31] With either of these egg meals GE is abnormal if greater that 50% of the meal is retained at 2 hours or greater than 10% at 4 hours.

Normal values must be established not only for the meal but also for the method used for image acquisition and processing. GE is dependent on body position, smoking, gender, phase of the menstrual cycle, and on the time of day the test is performed.[32-34] Medications such as prokinetic agents, antisecretory drugs, gastric acid suppression, and narcotics can affect GE. Supine positioning can significantly slow gastric emptying of solids.[35] Computer regions of interest corresponding to the stomach are defined to obtain the gastric counts. Because of the complex and changing shape of the stomach, automated methods for thresholding and edge detection have still not been commercially developed and manual regions of interest are in common use.

The simplest approach to interpreting gastric-emptying data has been to report the time to 50% emptying of the meal ($T_{1/2}$) or to use the percent of emptying measured at fixed times after meal ingestion. Until recently GE studies were commonly performed only up to 2 hours after meal ingestion. Recent studies however have shown that the percent retained at 4 hours is most reproducible[36] and detects more patients with abnormal GE.[31] However, debate still exists on how long GE studies should be performed and what is the optimum parameter for quantifying GE.

Role of Other Specialized Tests of Gastric Function

GE is found in a significant number (30-70%) but not all patients with dyspepsia. It is estimated to occur in 20% to 40% of diabetic patients, particularly those with long-duration, type 1 diabetes.[2] Given the low occurrence of documented delayed GE in symptomatic patients, it is increasingly recognized that special studies are needed to more completely evaluate the stomach, including separate fundal and antral motor function, fundic relaxation, visceral hypersensitivity, antroduodenal coordination, and gastric dysrhythmias.[37-39] In addition, psychosocial factors are important and, in at least one study, appear to correlate better than objective measurements of gastric physiology.[40] New therapies for dyspeptic symptoms now are being developed to target multiple potential causes.[36]

Bicompartmental (Fundal–Antral) Gastric Emptying

Regional analysis of GE should be included as a part of the clinical interpretation of GE studies. Inspection of the fundal and antral gastric activity in the images and quantification of regional emptying can be helpful for explaining dyspeptic symptoms especially when global GE values are normal. Studies have shown early satiety associated with early distal distribution of the liquid phase of a mixed solid-liquid meal and fullness associated with late proximal retention[41,42]

Previous studies of gender differences in GE have shown that women have slower gastric emptying. One study showed that this appeared to be caused by both increased proximal retention in the fundus as well as slowing of the terminal slope of the distal stomach in women.[43] However, other data show that antral retention correlates with dyspeptic symptoms in women.[44]

Studies of diabetics have shown that solid-food GE is most commonly delayed with the delay associated with increased retention of solids in the proximal stomach.[45] As opposed to slow GE, some studies have shown that there is accelerated emptying of high caloric liquid meals associated with diabetes.[46,47] This has been related to proximal stomach dysfunction and rapid fundal emptying of high caloric liquids and semisolids.[48,49]

Dynamic Antral Scintigraphy (DAS) and Electrogastrography (EGG)

Antral hypomotility is associated with symptoms of gastric stasis. Antroduodenal manometry has documented a lower motility index (number of contractions × the amplitude of contractions) for patients with neuropathic and myopathic causes compared with patients with idiopathic hypomotility.[50] Scintigraphy permits measurement of the frequency and amplitude of antral contractions as a part of a routine solid-liquid GE study. Normal antral contractions occur at a rate of 3 per minute. This 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 because of the retention of food in the fundus but also because of the decreased strength of antral contractions, which occur at a higher frequency.[51] A majority of patients with gastroparesis are women, with as much as 82% predominance in one large study.[26,52] Differences in normal male and female antral contractions have been documented. Using scintigraphy to measure antral contractions, Knight et al[53] found that woman have normal frequency but lower amplitude contractions not associated with hormone changes during the menstrual cycle. DAS can be particularly helpful to assess the pharmacologic effect of drugs on GE.[53]

Efficient GE is best achieved when there is antropyloroduodenal coordination so that the phasic antral contractions are appropriately timed with pyloric opening and duodenal peristaltic contractions. If there is antropyloroduodenal incoordination, the pyloric or duodenal contractions are out of phase with antral contractions and result in an increase in gastric outlet resistance that delays GE. There are few studies investigating the use of DAS to study this coordination, but a clear association of gastroparesis and response to prokinetic drugs can be demonstrated.[54]

EGG recordings provide information similar to DAS by measuring gastric myoelectric activity and provide information on the frequency and amplitude of antral contractions. EGG records gastric myoelectrical activity, known as the slow wave, using cutaneous electrodes affixed to the anterior abdominal wall. The slow wave is responsible for controlling the maximal frequency and the propagation of gastric contractions. The normal gastric slow wave frequency is approx-

imately 3 cycles/min. Meal ingestion increases the amplitude of the EGG signal, which is believed to result from increased antral contractility and distention of the stomach from a meal. EGG quantifies the dominant frequency and regularity of gastric myoelectrical activity, quantifies the percentage of time in which abnormal slow wave rhythms are present during fasting and postprandial periods, and assesses the increase in signal amplitude (or power) after a meal.

Gastric dysrhythmias (tachygastria, bradygastria) and decreased EGG amplitude responses to meal ingestion have been characterized in patients with idiopathic and diabetic gastroparesis.[55] Gastric myoelectric abnormalities have also been described in patients with unexplained nausea and vomiting, motion sickness, and nausea and vomiting of pregnancy. Data suggest that the EGG is complementary to scintigraphic GE for evaluating patients with dyspepsia. EGG abnormalities are present in 75% of patients with delayed GE versus 25% of symptomatic patients with normal GE. In one study of dyspeptic patients, 31% had abnormal GE alone, 31% had abnormal EGG alone, and 45% had an abnormality in either test.[56] Some investigators suggest that EGG abnormalities and delayed GE may define different patient populations with dyspeptic symptoms. EGG is considered an adjunct to GE scintigraphy as part of a comprehensive evaluation of patients with refractory dyspepsia. However, to date, there has been little investigation to validate directly the utility of EGG in the clinical management of patients with suspected gastric dysmotility.

Fundal Accommodation Studies

Fundal relaxation (accommodation) is a well-established physiologic response that allows the stomach to increased intragastric volume without increased intragastric pressure. The barostat is the current reference method to assess accommodation but has been criticized as invasive and nonphysiologic.[57] In addition to imaging techniques, nutrient or water loading tests also have been used to assess gastric filling capacity and sensation (visceral hypersensitivity). Patients with functional dyspepsia report fullness at lower volumes of ingested water and develop more symptoms than do controls. Water load volume better discriminates patients with dyspepsia from controls than does symptoms provoked during water load.[58]

Because the gastric mucosa accumulates ^{99m}Tc-pertechnetate after intravenous administration, this permits three-dimensional single-photon emission computed tomography (SPECT) volumetric imaging of the outer wall of the stomach. This has been validated as a noninvasive method to measure gastric volumes pre meal and at any time after meal ingestion.[59,60] It is also possible to simultaneously assess the relationship of liquid or solid meal emptying and gastric accommodation (Fig. 1). Such studies have shown maximal gastric volume change (mean = 185%) occurs immediately after mean ingestion which persists despite meal emptying.[61] It is expected that these new methods to measure gastric accommodation will be of clinical value especially to study patients with dyspepsia and normal GE parameters and may help direct medical therapy.

Pediatric Gastric Emptying

Delayed GE may be suspected in infants younger than 2 years of age who have vomiting, abdominal pain, or early satiety. In infants GE scintigraphy usually is performed combined with evaluation for GER with the patient's milk or formula feeding to which ^{99m}Tc-SC is added. Normal values for GE for infants for various meals have not been established because of lack of control studies. One excellent review discusses how quantification varies with patient positioning and meal composition. The data suggest that for children under two years of age meal size is less critical and a range of gastric retention for various liquid meals between 40% and 70% at 1 hour has been reported.[62]

GE studies are used to determine whether an added pyloroplasty at the time of fundoplication in children is needed. At least one study has shown that solids are more important than liquids in predicting postoperative delay of GE, which suggests that both solid and liquid normal values need to be established for these young patients.[63] Although scintigraphy has been considered the "gold standard" for pediatric as well as adult GE studies, other methods that avoid ionizing radiation are appealing and have been used to measure GE. Recent studies have shown a good correlation of ^{13}C breath testing and antral electrical impedance measurements with scintigraphic GE.[64,65] Ultrasound measurement of antral cross sectional area has been used to investigate gastric emptying in low birth weight infants.[66]

Other Competing Tests of Gastric Function

Real-time ultrasound has been used to assess GE in many studies and is especially attractive as noted previously for pediatric studies. Serial antral cross-sectional area usually is measured after ingestion of a liquid test meal and antropylorodouodenal motility and flow of liquid content can be measured. The test remains limited to use in a few centers as an investigational tool and remains very operator dependent and unable to quantitate solid emptying.[67]

Breath testing continues to be a noninvasive test that is popular in some centers for measuring GE because it is an office-based method that requires no exposure to ionizing radiation. ^{14}C or ^{13}C octanoic acid is bound to egg yolk. Breath samples are obtained every 10 to 15 minutes after egg ingestion. When the labeled solid empties the stomach, it is rapidly absorbed in the duodenum and then transported to the liver, where it is metabolized and ultimately excreted in the lungs as labeled CO_2. The test is limited if there is small bowel malabsorption or impaired pulmonary function. The AGA still recommends scintigraphic testing of solid GE as the gold standard for assessing GE.[2]

Magnetic resonance imaging is another method than does not use ionizing radiation. Because of the high spatial resolution, accurate measurements of total, proximal, and distal gastric volumes can be obtained. Using dynamic imaging pulse sequences frequency and amplitude of antral contractions and potentially antropyloroduodenal coordination can be assessed. The studies are time consuming and utilize very expensive equipment already in high demand in clinical centers. Its current use remains primarily for research.

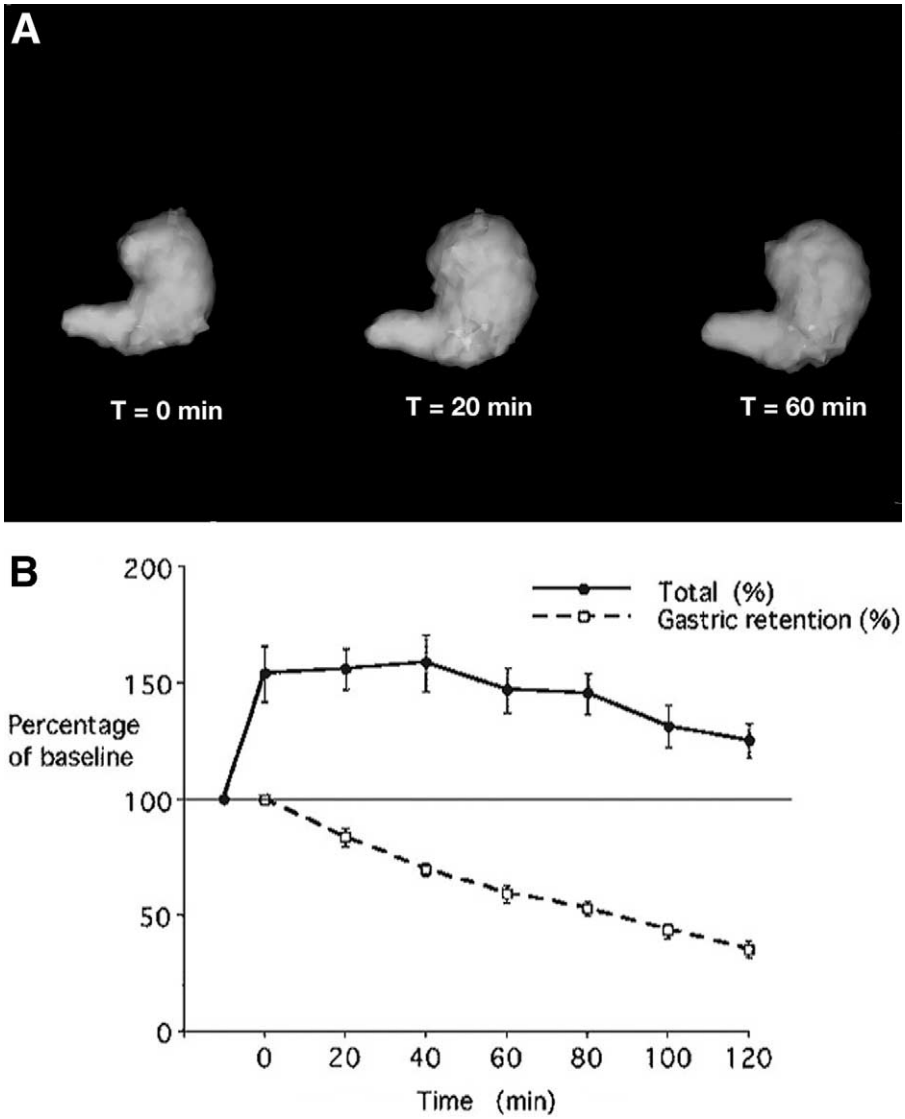

Figure 1 (A) SPECT 3-dimensional gastric accommodation study. These 3-dimensional volume-rendered images show fundal accommodation (increase in volume) that occurs early after meal ingestion (20 minutes) and that persists at 1 hour. (B) Simultaneous gastric emptying curve and SPECT total gastric volume (as a percentage of baseline volume) shows that the accommodation response persists for hours after meal ingestion despite gastric emptying of the meal.

Small Bowel and Colon Transit Studies

In many cases dyspeptic symptoms overlap such that it is difficult to differentiate the site of origin as originating in the upper- or lower-GI tract or both. It is now recommended that GI transit studies be used to localize the potential site of disease and guide therapy.[4] Recent studies have demonstrated motor dysfunction of multiple parts of the upper GI tract in diabetics.[68] Based on the need to evaluate motility throughout the entire GI tract, gastroenterocolonic or whole gut transit (combined gastric emptying and small bowel and colon transit) scintigraphy has been developed.

The ileocolonic junction is an important anatomic and functional landmark. It refers to that area of the distal small intestine that controls the influx of chyme into the colon. Specialized contractions in the distal small intestine are used to empty ileal chyme into the colon. They occur irregularly, usually in the fasted state.[69] Both a functional mechanical valve and a muscular sphincter at the ileocecal junction prevent reflux of colonic contents into the small bowel and permit storage of ileal chyme.[70] Although a meal may take 2 to 4 hours to pass from the pylorus to the ileocolonic junction (500 cm), it can take 12 to 72 hours to transit the 100 to 150 cm of the colon. Large migrating contractions in the colon occur only two or three times per day, leading to mass movements and defecation.[71]

Small Bowel Transit Studies

Measurement of small bowel transit (SBT) can be difficult because the input of a meal into the small intestine is dependent on GE and small intestinal chyme is spread out over a large distance as it moves toward the colon. Antegrade and retrograde movements of chyme occur and, although com-

plex and irregular at any given time, result in a net progression toward the colon.

The simplest scintigraphic method to measuring small bowel transit is to measure orocecal transit time. Precise definition of the initial arrival of activity in the cecum requires frequent imaging (every 10 to 15 minutes). Hydrogen breath testing correlates well with scintigraphy. In one study simultaneous orocecal transit times were 56 ± 4 minutes for lactulose breath testing and 43 ± 4 minutes for scintigraphy. Lactulose is not physiologic and significantly accelerates orocecal transit time.[72] Without lactulose, mean SBT time measured 220.9 ± 49 minutes with a range of 131 to 322 minutes. Significant intrasubject variability in small bowel transit however has been observed.[73]

It has been observed that isotope collects in a well-defined region of the pelvis proximal to the ileocolonic junction before passing into the colon. This buildup of activity in the terminal small bowel occurs because the terminal ileum functions as a reservoir for chyme before it passes into the colon.[70] A simplified scintigraphic measurement of SBT does not attempt to characterize the complex temporal or spatial peristaltic small bowel contractions but rather measures the bulk movement of volume distally into the terminal ileum or proximal colon.[74,75] The rate of isotope accumulation in the terminal ileum can be used as an index of small bowel motility.[76] A simple index of SBT is measurement of the percentage of administered activity that has accumulated in the terminal ileum at 6 hours after meal ingestion. When ^{111}In-DTPA in water is given with a 2 whole-egg GE study, normal small bowel transit is present if >40% of administered activity has progress into the terminal ileum and/or cecum and ascending colon at 6 hours.[77] Others have used a measure of proximal colonic filling.[78]

Colon Transit Studies

Therapy for patients with chronic constipation depends on identifying whether there is slow colon transit, pelvic floor dysfunction, or irritable bowel syndrome. Imaging of colon transit can be performed using serial radiographs and radiopaque markers. The markers are ingested with a meal, and radiographs are obtained to count the number of markers in segments of the colon. Although these markers are nonphysiologic, compared with intestinal chyme, the rate of transit is size dependent and intracolonic localization can be difficult with limited anatomic landmarks; they correlate well with scintigraphic measurement of colon transit.[79,80]

^{111}In-DTPA remains an ideal agent for colon transit scintigraphy. It is nonabsorbable and has a long half-life to permit several days' imaging. To quantitate colon transit, the geometric center (GC) has been defined to measure the progression of colonic activity.[81] To calculate the GC, the colon is divided into anatomic regions each with a numerical value: cecum-ascending colon (1), hepatic flexure, (2), transverse colon (3), splenic flexure (4), descending colon (5), rectosigmoid colon (6), and excreted stool (7). The GC is a weighted average of the counts in each region. A low GC (1-2 indicates that the center of the activity is in the proximal colon, and a higher GC (5-7 indicates that it has progressed to the left side of the colon or has been eliminated in the stool. With this approach, a simple, single numerical value is used to measure the transit of activity through the colon.

Two methods that use oral ^{111}In-DTPA to measure colon transit are in clinical use. One (Mayo Clinic, Rochester, MN) requires preparation of a resin-coated capsule that is designed to dissolve at a pH between 7.2 and 7.4 in the environment of the ileum (pH = 7.4).[82] A simpler alternate method (Temple University, Philadelphia, PA) is to give the ^{111}In-DTPA as a part of a standard solid-liquid GE meal.[76] Using the solid-liquid meal, the normal mean (± 1 SD) GC values are 4.6 ± 1.5 at 24 hours, 6.1 ± 1.0 at 48 hours, and 6.6 ± 0.19 at 72 hours.

In practice, one should image the colon at 24 and 48 hours. If the GC at 48 hours is less than 4.1 (proximal to the splenic flexure), no further imaging is needed because colon transit is delayed. If the GC is greater than 4.1 but less than 6.4, an image at 72 hours should be obtained to exclude functional outlet obstruction. There are 3 patterns of slow colon transit: generalized slow transit with diffuse retention throughout the colon; right-sided retention proximal to the splenic flexure (colonic inertia), and retention in the rectosigmoid (functional rectosigmoid obstruction)[83] In patients with diarrhea, accelerated colon transit can be confirmed with a GC greater than 6.1 (at or beyond the rectosigmoid) at 24 hours.

Using similar geometic center analysis and ^{111}In-labeled polystyrene (cation exchanger) micropellets other investigators have shown that therapy can be directed by differentiating slow colon transit from outlet obstruction.[84] Colon transit scintigraphy has been used to demonstrate the prokinetic effect of drugs.[85,86] The constipating effects of calcium channel blockers and analgesic drugs have also been documented with scintigraphy.[76,87]

Whole-Gut Transit Studies

Whole-gut transit scintigraphy (WGTS) combines measurement of GE, SBT, and colonic transit after the administration of a dual-isotope solid-liquid meal. These studies are helpful for evaluating patients whose symptoms cannot be classified as either upper or lower GI in origin or where a functional, not an organic cause is suspected. Patients with diarrhea-predominant irritable bowel syndrome have shorter small bowel transit and rapid colonic filling, whereas constipated patients have slower SBT and delayed colonic filling.[75] In a study at the Mayo Clinic, 40% of patients referred for upper-GI symptoms, constipation, or diarrhea were found to have an organic cause of symptoms but 60% were diagnosed as functional.[88] Colon transit is slowed more commonly in patients with organic disease and normal in patients with functional constipation. In a study to evaluate the clinical utility of WGTS at Temple University, organic disease was found in many patients with an initial suspected functional disorder and the initial diagnosis was changed in 45% patients and patient management was changed in 67% patients.[77]

Symptoms related to colonic dysmotility usually include abdominal pain, constipation, or diarrhea. WGTS appears

most helpful for evaluating patients with constipation. Many patients with severe idiopathic constipation have prominent upper-GI symptoms. It is important to exclude significant upper-GI dysmotility in such patients before surgery because subtotal colectomy may not correct their symptoms.[89] Colectomy should be performed only if a transit abnormality is limited to the colon. VanDerSijp and associates[90] studied a group of patients with severe idiopathic constipation with upper-GI symptoms. They found that of 12 constipated patients, 3 of 4 with upper-GI symptoms had abnormal gastric emptying and SBT in addition to delayed colon transit. The presence of abnormal GE, SBT, and colon transit abnormalities together suggest a diagnosis of chronic idiopathic intestinal pseudoobstruction.

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