Original Article

Gastric Emptying Scintigraphy: Beyond Numbers – An Observational Study to Differentiate between Various Etiologies and a Step toward Personalized Management

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Abstract

Aim: Gastric emptying (GE) scintigraphy is commonly used as a standard diagnostic procedure for the assessment of functional dyspepsia (FD). Results of the study are often reported as either normal or delayed GE times. The aim of this study was to recognize various patterns of scintigraphy among both normal and abnormal emptying times. **Materials and Methods:** Fifty patients with suspected FD were included in the study. GE study was performed with a standardized vegetarian solid meal. **Results:** Out of 50 patients, 33 patients had deranged GE. Thirty patients had delayed GE. Three patients demonstrated gastric hurrying. Five different patterns were demonstrated in patients having similar emptying and retention times such as reduced fundus compliance, decreased fundic accommodation, antral dysmotility, gastric hurrying, and gastroesophageal reflux. **Conclusion:** According to our findings, it may be suggested that visual assessment of GE and identification of various pattern is a very important aspect of the GE study. It not only subcategorized patients but also decreases the number of "normal" studies. This finding may have an impact on patient management in the era of personalized medicine.

Keywords: *Antral dysmotility, fundic compliance, gastric emptying study, gastroparesis, intragastric meal distribution*

Introduction

Functional dyspepsia (FD) is a common disorder and can markedly impair patients. It is a heterogeneous disorder, with different pathophysiological mechanisms underlying various symptom patterns. Various diagnostic modalities are used in the evaluation of dyspepsia; however, the diagnostic yield of these test are variable. Gastric emptying (GE) remains one of the most widely available tests for the assessment of stomach functions physiologically. The result obtained by the study usually shows impaired GE, but different etiologies are not classified.

Materials and Methods

Subjects

This retrospective study was conducted in the departments of nuclear medicine, from January 2017 to December 2017. Patients with suspected FD referred for solid GE study were included in this study. Total 50 patients were included in the study referred for various symptoms suggestive of FD.

Test meal

Culturally acceptable, vegetarian solid meal which was easy to prepare was used for the study. Vegetarian meal has been standardized in a previous study.[1] 99mTc sulfur colloid was prepared by sodium thiosulfate method. Wheat flour (25 g) was mixed with 10–20 mL of water containing 500 μCi 99mTc sulfur colloid (l–2 mL). The dough was rolled into round breads and roasted on a heating pan to prepare Indian bread or "chapatti." Stability of this food-radionuclide compound had been established. The rest of the meal was prepared on premises and concurrently on the day of the study. It consisted of rice (25-g uncooked weight) and black gram (25-g uncooked weight) with cooking oil (1.5 g) added. Calorific value of this meal was 280 Kcal with 70% carbohydrate, 14% protein, 8% fat, and 8% fiber. The study was performed in the morning after an overnight or at least 6-h fasting. All

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participants consumed the whole test meal within 10 min. Only 2–3 small sips of water were allowed. The time taken to ingest the meal was recorded. Furthermore, the note was made if portion of the meal was left behind.

Gastric emptying scintigraphy

GE study was performed in accordance to the procedure laid down by the joint guideline of society for nuclear medicine, the American Neurogastroenterology and Motility Society.[2] Patients were scanned under a dual-head gamma camera (Infinia Hawkeye 4, GE Healthcare, Buckinghamshire, United Kingdom) set at 99mTc window (140 keV ± 15%) in the supine position to visualize the whole stomach; simultaneous anterior and posterior radioactivity measurements were obtained. After ingestion of the radiolabelled test meal, patients were positioned supine on a dual-head gamma camera. Static image of one minute duration was done immediate post meal followed by serial static images at 30, 60,120,180 and 240 minutes. Between imaging sessions, the participants were accommodated in a designated waiting area. No other food was allowed during the study.

Image analysis and quantification of gastric emptying

Image interpretation was performed in accordance to the procedure laid down by the joint guideline of society for nuclear medicine, the American Neurogastroenterology and Motility Society.[2] For each image taken, the gastric region of interest was drawn manually. The geometric mean of the anterior and posterior gastric counts for each time point was calculated and corrected for 99mTc decay (6.02 h half-life) where the geometric mean count = (anterior counts × posterior counts)½. The final results are expressed as a percentage of radioactivity remaining in the stomach at each time point with the total gastric counts normalized to 100% for the time t = 0 (first image set was obtained immediately after meal ingestion). Several parameters of GE were individually calculated for each participant. Images were analyzed qualitatively as well as semiquantitatively; t½ and percentage gastric retention at 1 h and 4 h were calculated for all the patients. If gastric retention was >60% at 2 h or >10% at 4 h, it was considered as delayed GE.

Results

Out of 50 patients, 33 patients had deranged GE. Thirty patients had delayed GE (gastric retention >10% at 4 h). Mean GE time (t½) was 164 min (100–362 min). One-hour retention was 80% (45%–100%). Four-hour retention was significantly high with a mean of 30% (16%–64%). A total number of patients having mean GE time (t½) >100 min were 34 in numbers. Out of these, 30 had delayed GE. Three patients demonstrated gastric hurrying. Mean GE time (t½) was 34 min. One-hour retention was only 22%.

We further analyzed our scan findings on the basis of image interpretation rather than quantitative parameter alone. We found that various distinct patterns were noted in patients having similar emptying and retention times [Table 1]. This may have a greater impact on the management of the patients. Out of 17 patients who had normal GE time, five patients were found to have reduced fundus compliance. Gastroesophageal reflux (GER) and grossly dilated stomach were noted in one patient. Although these patients had near-normal GE as per 4-h retention criteria (10%), emptying half time was raised.

We represent few representative cases having patterns such as decreased stomach accommodation, fundus dysmotility, dilatation of the stomach, gastric hurrying, sluggish gastric as well as bowel emptying, and GER.

Cases and Discussion

Reduced fundic compliance

Reduce fundic capacity was noted in eight of our patients [Figure 1]. We observed this scan finding even in symptomatic patients showing overall normal GE times [Figure 2]. Dilatation of funds with food "accommodation reflex" is an important mechanism of normal gastric physiology. In FD, impairment of accommodation has been found up to 40% of cases.[3] The accommodation reflex provides a temporarily store for ingested food before controlled release into the intestine occurs. It consists of a reduction in gastric tone and an increase in compliance in response to food intake, allowing for an increased fundic volume without accompanying rise in intragastric pressure.[4] The symptom most closely associated with impaired gastric accommodation is early satiety, and weight loss may be a long-term consequence. Various investigation has been used to evaluate gastric volume such as barostat, single-photon emission computed tomography (SPECT) nuclear scintigraphy, ultrasonography, and magnetic resonance imaging. A recent study has demonstrated that

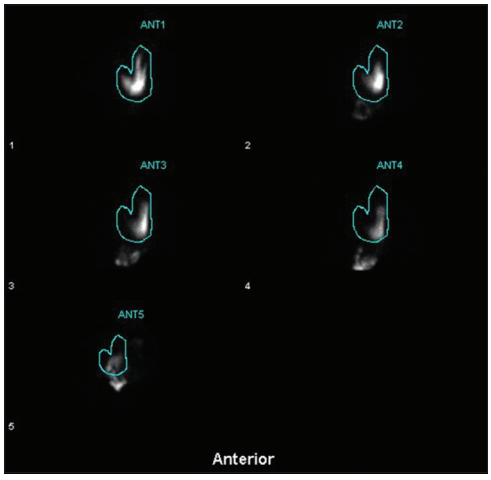

Figure 1: Impaired fundic accommodation with significantly delayed gastric emptying. There is decreased activity in the fundic region with visualization of antropyloric region at T0. Gastric emptying is significantly delayed (4-h retention ~31%). Stomach appears to be distended with no significant movement of the tracer in the small bowel even at 1 h of the study

impaired fundic accommodation can be assessed visually during routine GE scintigraphy (GES) with moderate agreement and high reader consistency. Visual and quantitative assessment can yield additional information on gastric motility to help explain patient symptoms.[5]

Abnormal distribution of the gastric content

This was the most common scan finding found in our group of patients. We found that several patients had abnormal distribution of the meal in the first image itself, for example, appearance of the pylorus and decreased uptake in the fundic region. This finding was seen even in few patients with overall normal GES based on percentage emptying criteria [Figure 3]. Over-distension of the antrum as noted in the postprandrial image may be responsible factor for dyspepsia. Ricci *et al*.[6] reported a distended fasting antrum and an increased postprandial antral volume in patients with FD as compared with healthy controls, suggesting that an impaired motor function of the distal stomach is present in a subgroup of patients with FD. This finding was confirmed by few subsequent studies.[7,8] In a study done by Caldarella *et al*., authors demonstrated a possible role of antrum in pathophysiology of dyspepsia by playing a dual role: acting as a faulty primer of reflexes and as a symptom-producing target. They also proposed that alternative therapeutic options such as antral contractile agents might prevent overfilling so that antral wall tension could then be kept below the symptom threshold.[9]

Antral dysmotility

In one of our patient, this scan finding was noted. There is a significant visualization of activity in the antropyloric region at T0. GE was significantly delayed with persistent visualization of the antrum at 4 h of study [Figure 4]. This rapid and persistent retention of food into the antrum may lead to several symptoms. Antrum has a very important part to lay once food moves in it. 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 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.[10] It has been demonstrated that increased antral contractions play an important role in postprandial nausea in FD.[11]

Gastric hurrying with dumping syndrome

In our series, we observed this finding in three patients [Figure 5]. One of them had not only fast GE but also rapid gastrocolic transit and appearance of the large bowel within 2 h of the study [Figure 6]. This phenomenon has been associated with diabetes mellitus (DM), and in addition, many idiopathic cases have also been reported. DM of recent onset may be associated with rapid GE. This occurs, especially in Type II DM, where early Wallerian degeneration and early vagal nerve damage are hypothesized.

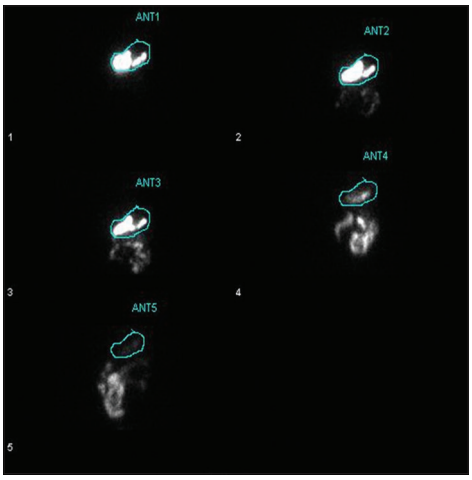

Figure 2: Impaired fundic accommodation with overall normal gastric emptying. There is significantly reduced compliance of the fundic region with overall normal gastric emptying (4 h retention <10%). No significant movement of tracer is noted into the small bowel even after 1 h of the study

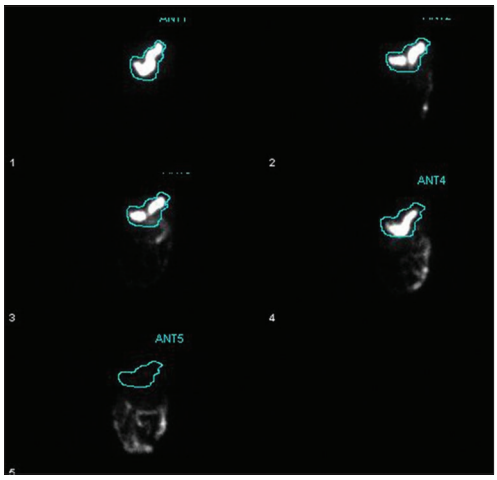

Figure 3: Abnormal distribution of the gastric content. There is an appearance of significant activity in the antropyloric region in the first image itself (T0). Although overall gastric emptying is normal (4 h retention ~ 3%)

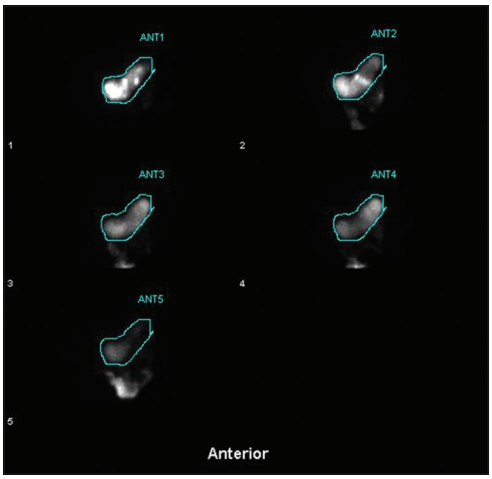

Figure 4: Antral dysmotility. There is significant visualization of activity in the antropyloric region at T0. Gastric emptying is significantly delayed (4 h retention ~41%). Stomach appears to be distended. There is persistent visualization of the antrum at 4 h of study

The presenting symptoms, in this case, may be essentially indistinguishable from the symptoms of gastroparesis, except that there are more vomiting in gastroparesis and more diarrhea in dumping syndrome (DS).[12] Almost half of the idiopathic patients could identify viral illness heralding the onset of chronic dumping symptoms. It has been proposed that in patients having classic postprandial symptoms of DS, a GE study may be performed to establish the diagnosis of DS, even in the absence of any preceding gastric surgery.[13]

Reduced volume of the stomach

Drinking capacity is often reduced in FD. Drink tests have been used for diagnosis of drinking capacity. Drinking capacity is mainly determined by antral volume, with a reduced antral filling in dyspepsia compared to healthy volunteer. The persisting symptoms of bloating, pain, and fullness in dyspepsia are predominantly associated with proximal stomach volume.[14] We have observed reduced fundic capacity in many patients. This pattern has been noted even in patients with normal GE time [Figure 7]. Similar findings have been noted by few studies; however, few studies have demonstrated that gastrointestinal (GI) symptoms are neither associated with antral distension nor with GE.[15,16]

Gastroesophageal reflux disease

Relationship between delayed GE and Gastroesophageal reflux disease (GERD) is still controversial, with few studies reported a significant association between the two whereas few show no significant relation.[17-21] However, demonstration of significant GER on GE study may lead to an alternating explanation of atypical symptoms of the dyspepsia. In one of our patients, we were able to see lower esophagus at T0 image, which lead to the diagnosis of GERD. GE times were normal in this patient [Figure 8].

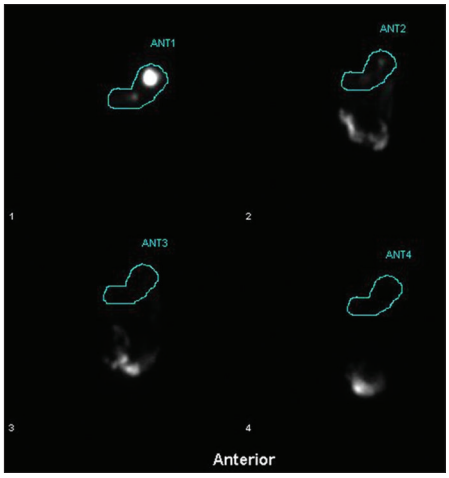

Figure 5: Gastric hurrying. There is normal visualization of the fundic activity at T0. One hour image revealed swift gastric emptying (1 h retention ~ 15%). No significant activity is noted in the stomach at 2 h images

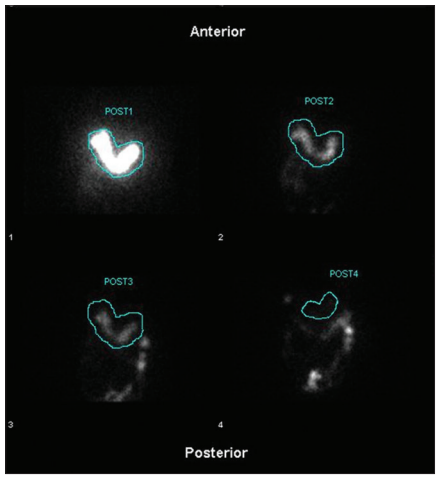

Figure 6: Gastric hurrying with visualization of the large bowel. There is normal visualization of the fundic activity at T0. One-hour image revealed near-normal gastric emptying (1-h retention ~ 40%); however, there is very rapid movement of the tracer into the small bowel. Delayed images taken at 2 h revealed gastric retention only ~ 10% with visualization of the large bowel. (Posterior images for better visualization of the large bowel)

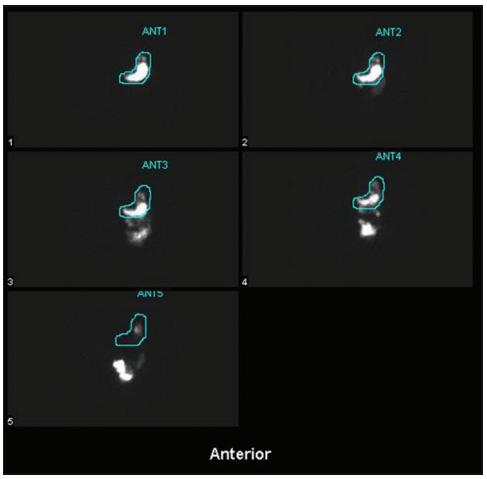

Figure 7: Reduced gastric capacity and normal gastric emptying. There is a faint visualization of the fundic activity at T0. Delayed images revealed near-normal gastric emptying (1-h retention ~ 40%). However, a patient had postprandial symptoms and was not able to finish his test meal completely

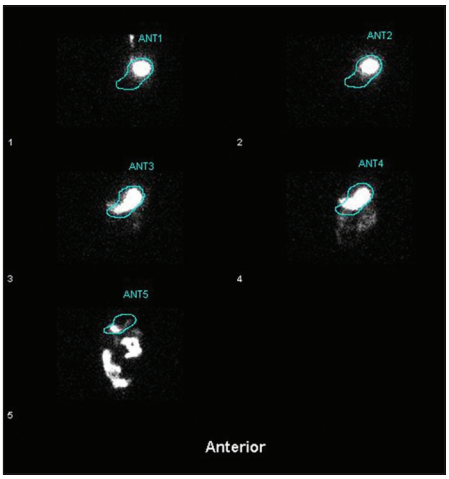

Figure 8: Gastroesophageal reflux. There is normal visualization of the fundic activity at T0. However, abnormal retention of activity is noted in the distal esophagus. There is normal drainage of the gastric content into the small bowel

Table 1: Patterns noted in the gastric scintigraphy

Scan pattern	Number of patients
Reduced fundic compliance	8
Abnormal distribution of the gastric content	16
Antral dysmotility	1
Gastric hurrying	3
Gastroesophageal reflux	1

Discussion

FD is a common disorder and can markedly impair the patients' quality of life. Based on the Rome III classification criteria, the main symptoms of FD consist of bothersome postprandial fullness, early satiety, epigastric pain, and epigastric burning.[22] In 2016, Rome IV criteria defined that the diagnosis of gastroduodenal disorders into the four categories: (1) FD, (2) belching disorders, (3) nausea and vomiting disorders, and (4) rumination syndrome. They define FD by 1 or more of the following: postprandial fullness, early satiation, epigastric pain, and epigastric burning, which are unexplained after a routine clinical evaluation, and include two subcategories: postprandial distress syndrome that is characterized by meal-induced dyspeptic symptoms and epigastric pain syndrome that does not occur exclusively postprandially.[23]

It is a heterogeneous disorder, with different pathophysiological mechanisms underlying various symptom patterns. Many changes in GI tract function and structure have been described in FD.[24] These involve impaired gastric accommodation,[25] delayed GE,[26] visceral hypersensitivity,[27] duodenal hypersensitivity to the luminal contents,[28] small bowel dysmotility, psychological disturbances,[29] *Helicobacter pylori* infection,[30] duodenal low-grade inflammation, mucosal permeability, food antigens,[23] and acute infections.[31]

Various diagnostic modalities are used in the evaluation of dyspepsia, such as upper GI endoscopy, *H. pylori* testing, GE studies (scintigraphy, c13-octanoic acid breath test, spirulina breath test, paracetamol absorption test, wireless motility capsule, and ultrasound), gastric accommodation (SPECT and barostat), gastric sensory function, myoelectrical activity, antroduodenal manometry, and symptom assessment questionnaires.[32]

GE remains one of the most widely available tests for the assessment of stomach functions physiologically. There is great variability between protocols followed among different laboratories. The variability in GES protocols may have a significant effect on patient management, as results may be inaccurate.[33] The most common findings noted and reported remain gastric emptying time and percentage emptying. One large meta-analysis of 17 studies with 868 patients and 397 controls found a significant delay of solid GE in approximately 40% of cases.[34] In a single-institution study, patients completed a standardized patient assessment of GI symptom questionnaire for 2 weeks before GES and during the GE study. This study found that symptoms of stomach fullness, bloating, and abdominal pain were higher in patients during GES with delayed GE than in patients with normal GE.[35] Our findings of delayed GE in approximately ~60% of the patient and rapid GE in ~6% patient correspond to the larger studies as mentioned above. We additionally noted abnormal image finding with overall normal GE in 8 patients. Its significance is not known. In few of the patients, two scan findings were noted such as large capacity stomach with antral dysmotility.

Management of functional dyspepsia and possible diagnostic utility of scintigraphy finding

The management of patients with FD starts with reassurance and education about the possible pathophysiological and risk factors associated with FD. Lifestyle and dietary recommendations may be helpful. Avoidance of drugs and foods such as nonsteroidal anti-inflammatory drugs, coffee, high-fat foods, alcohol, and smoking is commonly recommended.[23] Identification of *H. pylori* infection is appropriate, as prospective trials indicate that eradication therapy is curative in approximately 1 in 10 infected patients. If the patient is not infected, then an empirical trial of acid suppression is justified to suppress symptoms related to an atypical presentation with GERD.[23] Pharmacological treatments for FD are more effective than placebo in randomized controlled trials. These include acid suppression, H2 receptor antagonists, prokinetics, herbal preparations, and antidepressants.

We recommend that all patients having abnormal GE emptying time and distinct scintigraphy pattern may be managed based on scan finding. Patients showing reduced fundic compliance with normal or abnormal GE may be given drug specifically targeting it. One placebo-controlled study has demonstrated that acotiamide significantly increased both gastric accommodation and GE in FD patients.[36]

Patient with sluggish GE may be given prokinetic drugs preferably. Only limited data are present for the dopamine 2 antagonists such as domperidone and metoclopramide although they are prescribed extensively.[24] However, owing to cardiac and neurological side effects, the use of these medications for long-term treatment is not recommended.[37] Itopride is a D2 antagonist and acetylcholinesterase inhibitor, which is marketed in some Asian countries. Most of the studies have shown good efficacy and symptom improvement with a low rate of adverse reactions with it.[38,39]

Patients having normal GE are more likely to have a component of visceral hypersensitivity or altered pain perception. These patients may be treated with drugs that can modify stimulus perception. Antidepressants may

potentially modify several components in FD such as treating underlying psychiatric condition (e.g., depression and anxiety), influencing central processing of pain stimuli, and increasing the perception threshold peripherally. Meta-analysis of antidepressant and anti-anxiety agents of 13 studies found that in 11 studies participants showed symptom improvement.[40] Patients presenting with rapid GE are unlikely to show response with prokinetic drugs.

Conclusion

FD is a complex disease. Multiple pathophysiological mechanisms can be involved, and there may be significant overlap with psychiatric and functional GI disorder. Available pharmacological agents target specific symptom and often multiple drugs are prescribed. Studying the pathophysiology may help to understand the disease process better and further guide management in a more scientific manner. GES may help in subdividing patients physiologically, which may allow for a better therapeutic approach. Targeting a specific pathology may have better outcomes rather than treating with nonspecific drugs.

There are several limitations of our study. First, the population studied is small and has a very high prevalence of abnormal GE. The utility of GE in a large population with a low prevalence of delayed GE needs to be tested. We have not correlated patient symptom with the scan types we identified in our patient groups. A large prospective randomized controlled trial will be needed to evaluate the response of treatment based on functional imaging.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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