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Noninvasive Measurement of Gastric Accommodation by SPECT

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Definition and Physiology of Gastric Accommodation

Accommodation of the human stomach to a meal is a specialized motor function of the gastric corpus and fundus enabling high volume increase with minimal rise in intragastric pressure[1, 2]. This gastric function enables humans to ingest relatively large amount of solid or liquid meals without producing any postprandial symptoms such as vomiting.

Gastric accommodation response is a predictable and robust reflex in health and it is mediated by vagal nonadrenergic, noncholinergic pathways that include a nitrergic synapse[3, 4]. A reduced gastric accommodation response can be seen in a variety of conditions such as functional dyspepsia, post-fundoplication dyspepsia, postvagotomy/gastric surgery, rumination syndrome and possibly, diabetes mellitus associated with vagal neuropathy[5-11]. Measurement of gastric accommodation may facilitate our understanding of the cause of upper GI symptoms in the postprandial period in functional and neuropathic diseases[7, 12-14], thereby impacting the outcomes of treatment.

Measurements of Gastric Accommodation

To measure gastric accommodation to a meal, barostat, ultrasound, MRI and SPECT have been proposed[15].

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1. Barostat

Barostat involves the placement of a polyethylene balloon into the stomach and linking it to a barostatic device to measure intragastric volumes in the fasting and postprandial periods[5]. The barostat and intragastric polyethylene balloon provide an excellent method to study viscus tone and visceral hypersensitivity.

However, tube replacement itself is invasive in nature and can cause discomfort to patients, thereby limiting its role to research laboratory. Moreover, the barostat-controlled balloon cannot accurately measure posprandial accommodation of the entire stomach and the intragastric balloon itself may interfere with the intragastric handling of the meal[16].

2. Ultrasound

Ultrasound studies of the proximal stomach allow non-invasive monitoring of meal induced relaxation of the proximal stomach[17]. The experience about ultrasound has been largely substantiated by Gilja et al.[17-20] Recently, three-dimensional ultrasound is being developed to measure proximal gastric volume[19], even though it is not yet widely available and requires further validation. However, the disadvantages of ultrasound are that it seems labor-intensive, requires a skilled sonographer and is likely to be observer-dependent.

3. SPECT (Single Photon Emission Computed Tomography)

This method was developed by Michael Camilleri et al. at Mayo Clinic[20]. This approach uses intravenous (i.v.) injection of a radioisotope, ^{99m}Tc-pertechnetate with SPECT imaging of gastric mucosa, followed by image processing and analysis using a software.

1) Principle

The gastric mucosa is able to take up and excrete ^{99m}Tc-pertechnetate from the circulating blood pool[22]. Both parietal (oxyntic) and nonparietal (mucous) cells can uptake this isotope. Therefore, this isotope is taken up in all parts of the stomach wall, despite regional differences in radionuclide incorporation because of variations in thickness or surface area of the gastric mucosa[23-25]. The stomach volume can be measured by imaging followed by three-dimensional reconstruction of the wall of the stomach.

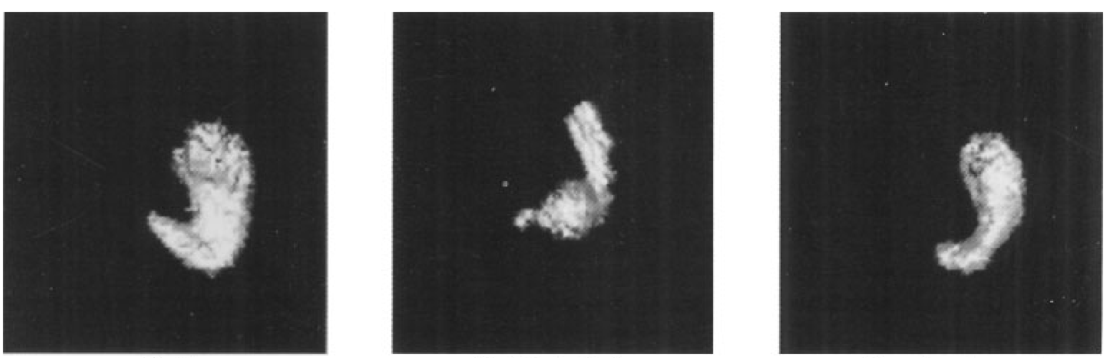
2) Methods

The initially used i.v. dose of ^{99m}Tc-pertechnetate was 20 mCi[21], but, later 50% reduction of i.v. dose of pertechnetate (10 mCi) was sufficient to visualize stomach. Radiation exposure is within permissible ranges for research and clinical studies. Tomographic images are obtained on a large field of view, dual-head-camera system (Helix SPECT System; Elscint, Haifa, Israel) equipped with low-energy, high-resolution collimators. Subjects are positioned supine on the imaging table with the detectors over the upper and mid abdomen to ensure imaging of the stomach and small bowel (Figure 1). Ten minutes after the i.v. injection of ^{99m}Tc sodium pertechnetate, tomographic acquisition is performed using the multiorbit mode of the system. Briefly, in this mode, the system performs three complete 360° orbits at 128 128 matrix, every 6° at 10 s/image. After completion of the acquisition, data from each orbit are reconstructed using filtered back-projection (Ramp-Butterworth filter, order 10, cut-off 0.45 Nyquist) to produce transaxial images of the stomach.

In order to evaluate gastric accommodation, gastric volumes are measured in fasting and postprandial state. Subjects or patients fast overnight before SPECT gastric volume test. SPECT image acquisition is performed 10 min after i.v. ^{99m}Tc-pertechnetate. After completion of acquisition in the fasting state, the supine subjects drink the test liquid meal with the aid of a straw over a 5-min period. Mayo Clinic has used 300 mL of Ensure® (Ross products, Division of Abbott Laboratories, Columbus, OH, USA) as a test liquid meal. After meal ingestion, two more camera orbits, each lasting 10 min, are completed; the total duration of imaging is 30 min.

3) Analysis

For the estimation of gastric volume, the transaxial images are transferred via DICOM to a desktop Windows NT (Microsoft, Redmond, WA) workstation. The stomach is identified in transaxial SPECT images using a semiautomated, intensity-based extraction algorithm (Object Extractor, Analyze^{AVW} PC 2.5) (Figure 1). This software system[26] has been used previously in volumetric imaging studies[27, 28]. Three-dimensional surface-rendered images of the stomach are produced and gastric volumes are measured using Analyze^{AVW}. Total gastric volume is measured during fasting and during the two 10-min postprandial periods. Mayo Clinic has used two parameters for the evaluation of the gastric accommodation; 1) the ratio of postprandial to fasting volumes and 2) the absolute volume change.



Healthy　Post-fundoplication　Non-ulcer dyspepsia

Figure 1. SPECT methods to measure gastric volumes. After 10 mCi i.v. of ^{99}mTc-pertechnetate, tomographic images are obtained on a large field of view, dual-head -camera system. They are three-dimensionally reconstruced by using a specialized software (Analyze program). See details in the text.

4) Validity

Intraobserver coefficients of variation in estimated fasting and postprandial volumes were 9 and 8%; interobserver variations were 13 and 12%, respectively[21]. Recently, the SPECT measurement of the volume change after a meal was validated in healthy subjects by simultaneous measurements by SPECT and an intragastric, barostatically controlled balloon[29]. There were significant correlations in the estimated postprandial gastric volumes (r=0.64, p=0.008) and postprandial to fasting gastric volume ratios (r=0.82, p<0.001) between the two methods.

5) Advantages

This novel accommodation test is noninvasive, does not require intubation and measures the accommodation of the entire stomach[16].

6) Pitfalls

Equipment for the SPECT test is not available in many centers, though it is available at many cardiac centers. Gastric sensation cannot be assessed by any of the imaging techniques, unlike with the barostat study. However, in the future, this test will be combined with a water/nutrient drink test[8, 16, 31-34] to assess sensation as symptoms.

Experiences of gastric accommodation measured by SPECT in various diseases

1. Nonulcer dyspepsia

Troncon et al.[30] used a radioisotope to evaluate the shape of the stomach and identified differences in intragastric distribution of a meal, suggesting that the fundus fails to accommodate postprandially in patients with functional dyspepsia. Jan Tack and his colleagues performed a barostat study and reported that impaired gastric accommodation to a meal was found in 40% of patients with functional dyspepsia[8]. The impaired gastric accommodation was associated with early satiety and weight loss. Kim et al.[35] applied the SPECT study to assess gastric accommodation in patients with idiopathic nonulcer dyspepsia and healthy subjects and to evaluate the application of three-dimensional (tomographic acquisition) SPECT in a tertiary referral center at Mayo Clinic. All patients also had gastric emptying study by gastric scintigraphy. Among healthy subjects (8M, 12F), the postprandial/fasting gastric volume ratio was 4.9 1.7 (mean SD, 5th through 95th percentiles 38, median 4.6). 13/32 (41%) patients with idiopathic nonulcer dyspepsia had reduced postprandial accommodation (the ratio <3) (Figure 2). Gastric emptying was fast in four (13%), normal in 25 (78%) and slow in three (9%) patients. Both tests were normal in 50% of patients. Weight loss of >10 pounds tended to be more frequently observed in those with reduced accommodation (62% vs 32%, p=0.09). The study illustrated that the impaired gastric accommodation is more common than delayed gastric emptying in dyspeptic patients in a tertiary clinical setting.

2. Obesity

Obesity, defined by an excess of body fat, is a highly prevalent disorder in the Western world[36]. Intragastric

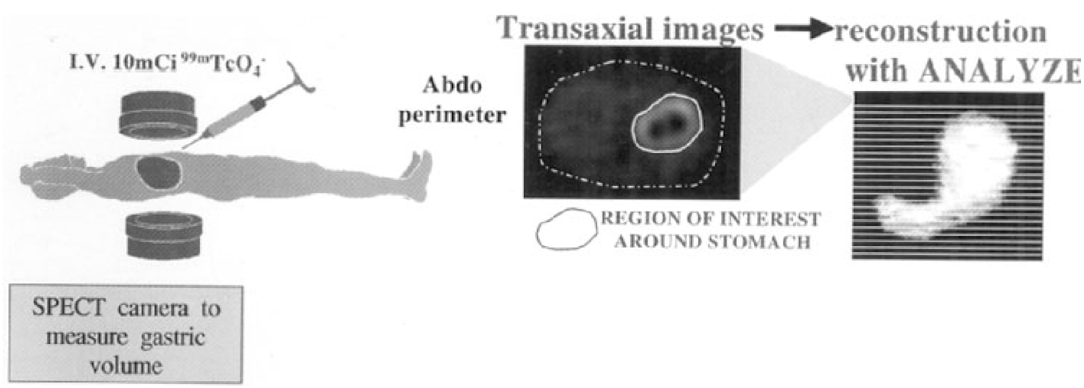


Figure 2. Examples of postprandial gastric images in participants from three groups: health, post-fundoplication and non-ulcer dyspepsia. Note the shape of the proximal stomach appears different in the participant with previous fundoplication; note also the overall reduction in gastric volume in the non-ulcer dyspepsia patient relative to the healthy control. However, the shape of the stomach in the patients with dyspepsia appears normal.

balloon studies showed that the gastric capacity was significantly larger[37-39] and the gastric capacity decreased after a restrictive diet in obese subjects[34]. However, inserting a gastric balloon or tube into the stomach and measuring the maximum water-filled balloon volume may reflect only an indirect index of gastric capacity. Furthermore, intubation itself may have evoked reflex relaxation of the stomach[16] or obese individuals may have had a more pronounced reflex relaxation in response to intubation, an artificial stimulus. Thus, Kim et al.[40] applied SPECT method and satiety test to compare gastric accommodation and satiety between 13 obese (BMI 30 kg/m^2, mean BMI: 37.0 kg/m^2) and 19 non-obese (BMI < 30 kg/m^2, mean BMI: 26.2 kg/m^2) asymptomatic subjects to prove the hypothesis that obese people had increased gastric accommodation and reduced post-prandial satiety. The satiety test measured maximum tolerable volume of ingestion of liquid nutrient meal (Ensure) and symptoms 30 minutes after cessation of ingestion. The results have shown that fasting and postprandial gastric volumes and the ratio of postprandial/fasting gastric volume were not different between asymptomatic obese subjects and control subjects. Maximum tolerable volume of ingested Ensure and aggregate symptom score 30 min later were also not different between obese and control subjects. Therefore, asymptomatic obese people did not show either increased gastric accommodation or reduced satiety and those data suggested that gastric physiology is unlikely to provide an important contribution to development of moderate obesity.

3. Post-fundoplication

After Nissen or laparoscopic fundoplication, patients frequently report upper abdominal (dyspeptic) symtoms. Theoretically, these symptoms may be the result of changes in function of the proximal stomach induced by fundoplication[11]. Smaller proximal stomach can be successfully documented by SPECT imaging in post-fundoplication patients[35, 41] (Figure 2) and Samsom et al.[42] reported that 2/4 post-fundoplication patients had total gastric volumes below those of healthy controls and could successfully documented. Kim et al.[41] also have shown by SPECT that 2/3 post-fundoplication patients had impaired gastric accommodation (the post-prandial/fasting gastric volume ratio< 3). These studies are in agreement with barostat studies and therefore, SPECT study may be potentially, clinically applicable in patients who complain of dyspeptic symptoms after fundoplication.

Potential drugs that have fundus-relaxing ability (Table 1)

Therapeutic approaches that restore normal post-prandial gastric accommodation are needed and should be tested in non-ulcer dyspepsia. A 5-HT_1 receptor agonist, sumatriptan, enhances the meal-induced relaxation in dyspeptic patients with impaired gastric accommodation[8]. Sumatriptan also improved symptoms of early satiety. Buspirone[43] and clonidine[44] are also fundus-relaxing drugs, however, long term studies seem warranted to confirm the therapeutic potential. Recently, a SPECT study has shown that a nitric oxide (NO) donor, isosorbide dinitrate, increased fasting gastric volume while erythromycin decreased postprandial gastric volume[45]. Cisapride[46] can also relax fundus through NO-mediated mechanism. Amitriptyiline may be one of the potential fundus-relaxing drugs and it decreases hypersensitivity, but it lacks evidence yet. Furthermore, we still lack the information of long term efficacy of these gastric relaxatory drugs. However, when we use these drugs, we have to take the effect of these drugs on gastric emptying into account; for example, sumatriptan[47] and clonidine may delay gastric emptying.

Table 1. Potential drugs that have fundus-relaxing ability.

Sumatriptan
Busprione
Serotonin selective reuptake inhibitors
Clonidine
Cisapride
NO donor, e.g., isosorbide dinitrate
Amitriptyline

Conclusion and Prospect

The noninvasive nature of the SPECT method as well as the rapidity of onset and consistency of the change in volume in the first 20 min postprandially suggested that the SPECT method may also be applied to assess the cause of postprandial symptoms in dyspeptic patients. This test holds great promise for measuring gastric response to a meal in clinical practice and in pharmacodynamic studies.

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