Development of a test to measure gastric accommodation in humans

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Kuiken, Sjoerd D., Melvin Samsom, Michael Camilleri, Brian P. Mullan, Duane D. Burton, Louis J. Kost, Timothy J. Hardyman, Benjamin H. Brinkmann, and Michael K. O'Connor. Development of a test to measure gastric accommodation in humans. Am. J. Physiol. 277 (Gastrointest. Liver Physiol. 40): G1217–G1221, 1999.—Postprandial symptoms of bloating, distension, early satiety, and nausea are associated with impaired postprandial gastric accommodation, which is detectable by means of an intragastric, barostatically controlled balloon in the proximal stomach and by ultrasound in the distal stomach. Our aim was to develop a noninvasive method to measure the entire gastric accommodation reflex. In 10 healthy volunteers, we used single photon emission computed tomography (SPECT) to measure fasting and postprandial gastric volumes. This method involved intravenous injection of 99mTc pertechnetate and gastric reconstruction of tomographic images with Analyze software. SPECT-Analyze imaging detects the postprandial gastric accommodation reflex in vivo. Mean fasting gastric volume was 182 ± 11 (SE) ml and mean postprandial volume was 690 ± 32 ml (P < 0.001). Both proximal and distal segments of stomach showed a two- to almost fourfold difference in volumes postprandially. Intraobserver coefficients of variation in estimated fasting and postprandial volumes were 9 and 8%; interobserver variations were 13 and 12%, respectively. SPECT-Analyze noninvasively measures postprandial gastric (total, proximal, and distal) accommodation in humans. This method appears promising to compare the accommodation response in health and disease and to perform mechanistic studies of the accommodation response.

The accommodation response to meal ingestion is a robust reflex in health. It results in a reduction in gastric tone and an increase in compliance, thereby facilitating the ingestion of large volumes of solids or liquids without inducing symptoms or the vomiting reflex. In several conditions, a reduced accommodation response appears to contribute to postprandial symptoms such as early satiety, distension, and weight loss. These conditions include functional dyspepsia, postfundic duplication dyspepsia, rumination syndrome, postvagotomy-gastric surgery, and possibly diabetes mellitus when associated with vagal neuropathy (1, 22–24, 28–30). As a result of increased wall tension and possibly stimulation of visceral afferents or alteration of cerebral perception, patients develop gastric hypersensitivity during fasting or postprandially (3, 7, 12, 13, 25, 27). These data suggest that measurement of accommodation may facilitate our understanding of upper gastrointestinal symptoms in the postprandial period and possibly enhance the choice of therapies in dyspepsia, Helicobacter pylori infection, and diabetes (8, 19, 24, 32).

Presently, the only reliable measurement of accommodation in the proximal stomach 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 (1). This invasive approach has been effective in research, but it is impractical and unlikely to be acceptable to most patients in clinical practice. Ultrasound has been used also to document antral accommodation. However, neither method can accurately measure accommodation of the entire stomach.

Previous studies have shown the feasibility of pertechnetate imaging of the gastric mucosa and even gastric wall motion when using dynamic scintigraphy; it is also possible to reconstruct two-dimensional images of the stomach using an edge detection method in an attempt to measure gastric volume (2, 15, 17, 18).

The aim of the present study was to assess the feasibility of three-dimensional (tomographic acquisition) single photon emission computed tomography (SPECT) to measure changes in gastric volume from the fasting to postprandial periods in healthy volunteers. Development of such a noninvasive test could introduce a novel approach for measuring gastric accommodation in clinical practice and in pharmacodynamic studies.

MATERIALS AND METHODS

Subjects. Ten healthy volunteers (5 male and 5 female; median age 38 yr, range 18–41 yr) were recruited from the local community by public advertisement. They were screened by means of an abridged bowel disease questionnaire to ensure that they had no gastrointestinal symptoms. The following exclusion criteria were applied: 1) no previous abdominal surgery except appendectomy; 2) no intake of medications other than stable doses of birth control pill, L-thyroxine, or estrogen replacement therapy; and 3) no intake of medications in the previous week that could alter gastrointestinal motor function. Females of child-bearing potential underwent a pregnancy test within 48 h of each study. All subjects gave their written informed consent to participate in the protocol, which had been approved previ-
ously by the Institutional Review Board and Radiation Safety Committee of the Mayo Clinic.

Imaging of gastric mucosa. The gastric mucosa is able to take up and excrete $^{99m}$Tc pertechnetate from the circulating blood pool (10). There is evidence that both parietal (oxyntic) cells and nonparietal (mucous) cells are capable of $^{99m}$Tc uptake. This property is now widely used to identify ectopic gastric mucosa in patients with suspected Meckel’s diverticulum and retained antral mucosa using radionuclide imaging (2, 10, 15, 21, 31). Uptake of $^{99m}$Tc pertechnetate is found in all parts of the stomach, although there could be regional differences in radionuclide incorporation due to variations in thickness or surface area of the gastric mucosa (2, 6, 31). In a previous study, Prather et al. (17) administered 5.0 mCi $^{99m}$Tc pertechnetate intravenously and noted sufficient uptake to allow the entire stomach to be visualized (17). To ensure sufficient visualization and quantification of volumes on tomographic images, we administered 20 mCi $^{99m}$Tc pertechnetate intravenously. Radiation exposure was within permissible ranges for research and clinical studies.

SPECT imaging. Tomographic studies were acquired on a large field of view dual-head gamma camera system (Helix SPECT System, Elscint, Haifa, Israel) equipped with low-energy, high-resolution collimators. Subjects were positioned supine on the imaging table with the detectors over the upper and midabdomen to ensure imaging of the stomach and small bowel. Ten minutes after the intravenous injection of 20 mCi $^{99m}$Tc sodium pertechnetate, dynamic tomographic acquisition was performed using the multifacet orbit mode of the system. Briefly, in this mode, the system performed 10 complete 360° orbits at 3 min per orbit. For each orbit, images were acquired into a 128 x 128 matrix, every 6° at 3 s per image. After completion of the acquisition, selected orbits could be summed to improve counting statistics. These orbits were then reconstructed using filtered back-projection (Ramp-Butterworth filter, order 10, cut-off 0.45 Nyquist) to produce transaxial images of the stomach.

Study design. Subjects were studied after an overnight fast. SPECT image acquisition was performed in all participants 10 min following intravenous injection of 20 mCi $^{99m}$Tc pertechnetate. After completion of two orbits, each lasting 3 min (baseline data or fasting state), the supine participants drank the test meal [300 ml of Ensure Plus (Ross Products, Division of Abbott Laboratories, Columbus, OH)] with the aid of a straw during the third orbit of the SPECT camera. After meal ingestion seven more camera orbits were completed, and the total duration of imaging was 30 min.

Data and statistical analysis. For estimation of gastric volume, the transaxial images were transferred via Interfile to a dedicated Unix workstation.

Stomach volume measurements were performed using the Analyze PC 2.5 (Biomedical Imaging Resource, Mayo Foundation, Rochester, MN) software system (9), which has been used previously in volumetric imaging studies (11, 14). To measure the volume of the stomach, it was necessary to identify the stomach in the transaxial SPECT images (Fig. 1) and separate it from the background noise. This was accomplished using a semiautomated segmentation algorithm (Object Extractor, Analyze PC 2.5), which requires the user to identify an appropriate seed point and grayscale threshold. Because $^{99m}$Tc pertechnetate is taken up by the gastric mucosa, the “fill interior holes” option was necessary to produce a solid stomach volume as opposed to a hollow shell. Three-dimensional renderings of the stomach were produced, and the user manually removed any extraneous structures, such as the upper duodenum or a kidney in close proximity to the stomach, which had not been removed in the segmentation algorithm. Total gastric volume was measured during fasting and during two postprandial periods (3–12 and 12–21 min). Volume changes between the fasting and two postprandial periods were calculated. To assess volume changes in the proximal and distal regions of the stomach, we arbitrarily divided the stomach by drawing a horizontal line across from the incisura.

Estimates of gastric volume were repeated to assess intra-(S. D. Kuiken) and interobserver (S. D. Kuiken and L. J. Kost) reproducibility. We calculated the coefficient of variation (CV) in the estimates of gastric volume by the same investigator on
two occasions (CV_{INTRA}) and by two separate investigators (CV_{INTER}). CV was calculated by the formula CV equals SD/overall mean, where SD is the standard deviation of differences between replicate estimates and overall mean is the grand mean of all gastric volume measurements during fasting or later postprandial period.

ANOVA was used to compare fasting, early, and later postprandial volumes; paired t-test was used to compare the magnitude of volume change between proximal and distal segments.

RESULTS

After thresholding out the background noise, a well-defined, three-dimensional image of the stomach was shown. The anatomic landmarks of the stomach could sometimes be easily identified to distinguish the proximal and distal parts of the stomach, as shown on a reconstructed image of the stomach (Fig. 2).

The outline of the fasting stomach (baseline volume) was also easily distinguishable from the background noise. In the early postprandial state, at 3–12 min after the meal (orbits 4–6), the stomach outline was difficult to define fully in 4 of 10 subjects, although volumes could be measured after digital processing of the images. A fluid level was visible in the gastric lumen showing secreted $^{99m}$Tc pertechnetate and indicating loss of radioisotope from the mucosa into the lumen in response to the meal. The late postprandial images (12–21 min after the meal, orbits 7–9) showed relatively well-defined outlines that allowed confident “thresholding” of the gastric wall from background and subsequent volume estimation. There was a significant increase in total gastric volume between fasting and postprandial periods in all subjects (P < 0.001, ANOVA, Table 1). The greatest volume increase postprandially was observed in the proximal stomach. The changes in gastric segment volumes postprandially were approximately two- to almost fourfold. The later postprandial volumes were not significantly different from early postprandial volumes within each segment (total, proximal, and distal stomach). However, the increase in volume in the later postprandial period was greater in proximal stomach (mean change 342%) vs. distal stomach (mean change 188%).

There were no significant differences in the repeated estimates of gastric volume performed by the same or by two separate observers (P > 0.2, paired t-test). The CV_{INTER} was 13% during fasting and 12% postprandially (12–21 min); CV_{INTRA} was 9% during fasting and 8% postprandially (Fig. 3).

DISCUSSION

In this feasibility study, SPECT was used to measure meal-induced volume changes in the stomach. The impetus for developing this method to measure gastric accommodation stems from the increasing evidence that defects in accommodation are frequently encountered in several dyspeptic syndromes (1, 22, 23, 26, 28–30). The development of the method also lends itself to noninvasively assess the physiological and pharmacological control of gastric accommodation. The technique combines established technology using tomographic imaging and image analysis with commercially available software. The noninvasive nature of the method as well as the rapidity of onset and consistency of the gastric accommodation response in the first 20 min postprandially suggest that the method may also be applied to assess postprandial symptoms in patients.

In this feasibility study, we elected not to perform a simultaneous barostat measurement of gastric accom-

<table>
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<th>Table 1. Gastric accommodation</th>
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<tr>
<th>Volume, ml</th>
<th>Total</th>
<th>Proximal</th>
<th>Distal</th>
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<tr>
<td>Baseline (fasting)</td>
<td>182 ± 11</td>
<td>131 ± 9</td>
<td>51 ± 7</td>
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<tr>
<td>Early (3–12 min) postprandial</td>
<td>655 ± 28*</td>
<td>518 ± 22*</td>
<td>137 ± 13*</td>
</tr>
<tr>
<td>Later (12–21 min) postprandial</td>
<td>690 ± 34*</td>
<td>561 ± 28*†</td>
<td>129 ± 12*</td>
</tr>
<tr>
<td>ΔVolume, ml</td>
<td>Early (3–12 min) postprandial</td>
<td>473 ± 27</td>
<td>387 ± 21</td>
</tr>
<tr>
<td>Later (12–21 min) postprandial</td>
<td>508 ± 32</td>
<td>431 ± 25</td>
<td>77 ± 12</td>
</tr>
<tr>
<td>%Volume change (3–12 min) postprandial</td>
<td>271 ± 29</td>
<td>313 ± 39</td>
<td>219 ± 51</td>
</tr>
<tr>
<td>%Volume change (12–21 min) postprandial</td>
<td>289 ± 26</td>
<td>342 ± 32</td>
<td>188 ± 38†</td>
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Values are means ± SE; n = 10 subjects. *P < 0.001 vs. fasting by ANOVA. †P = 0.07 vs. early postprandial. ‡P < 0.01 vs. proximal stomach.
The intraballoon pressure necessary to measure baseline and postprandial volumes with the balloon in place could conceivably introduce an element of artifact. Moreover, the location of a barostatic balloon influences the portion of the stomach that can be assessed, and this may vary in time and between individuals. We noted that the magnitude of the postprandial volume change (average 2 to 4 times fasting volume) measured in the stomach was comparable to changes observed in earlier reports using the barostatic method (20, 22, 25, 29). However, the imaging technique developed allows assessment of the entire stomach, unlike the balloon method and ultrasound which typically assess either the proximal or the distal stomach, respectively. In the later postprandial period, the SPECT method also identified a relatively greater accommodation of the proximal than the distal stomach, when expressed as a change from the fasting volume of the same segment.

We perceive that there are pitfalls in the division of stomach segments into proximal and distal regions. In particular, the incisura may not be pronounced, the two gastric compartments may not be easily identifiable, and somewhat arbitrary definitions (e.g., horizontal line from incisura) may not always apply. Moreover, because the gastric volume changes, a region of interest applied on fasting stomach may need to be modified for postprandial measurements. Further validation studies will be needed to more confidently use the method to assess regional accommodation.

The intra- and interobserver variances suggest that the current analysis appears robust. However, this feasibility study requires future validation, including simultaneous measurement with a barostatic balloon and documentation of the predictable effects of drugs that reduce the accommodation response, such as erythromycin, or drugs that enhance gastric relaxation, such as nitric oxide donors, α2-agonists and 5-HT1-agonists (3–5, 8, 25, 27). Image quality may also be enhanced in further studies by strategies aimed at improving the signal-to-noise ratio. Factors that determine signal quality include variation in the timing and dose of the intravenous technetium administration relative to the time of the meal and SPECT image acquisition. Mucosal 99mTc pertechnetate uptake and secretion may also be enhanced with the use of specific drugs (2, 21), including histamine H2-receptor antagonists, which reduce secretion and produce improved wall imaging. However, the latter drugs may conceivably alter some of the motor functions of the stomach (16). Hence, we believe that nonpharmacological enhancement of images will be preferable.

This method has a number of potential advantages over the more invasive barostatic method currently used predominantly in research studies. However, cost comparisons cannot be made yet and the SPECT method cannot simultaneously assess gastric sensation, unlike the intragastric balloon. The pros and cons of the two methods are summarized in Table 2.

In summary, we have developed a noninvasive measurement of gastric accommodation in humans; this novel test has potential for further in vivo physiolog-
cal, pharmacological, and clinical studies of gastric motor functions in humans.

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