Relationship of gastric emptying and volume changes after a solid meal in humans

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Burton, Duane D., H. Jae Kim, Michael Camilleri, Debra A. Stephens, Brian P. Mullan, Michael K. O’Connor, and Nicholas J. Talley. Relationship of gastric emptying and volume changes after a solid meal in humans. Am J Physiol Gastrointest Liver Physiol 289: G261–G266, 2005; doi:10.1152/ajpgi.00052.2005.—Noninvasive imaging has been developed to measure gastric volumes. The relationship between gastric emptying and volume postprandially is unclear. The aims were to 1) develop a 3-dimensional (3D) single photon emission-computed tomography (SPECT) method to simultaneously measure gastric volume and emptying postprandially, 2) describe the course of gastric volume change during emptying of the meal, and 3) assess a 3D method measuring gastric emptying. In 30 healthy volunteers, we used 111-In-planar and 99mTc-SPECT imaging to estimate gastric emptying and volume after a radiolabeled meal. A customized analysis program of SPECT imaging assessed gastric emptying. A Bland-Altman plot assessed the performance of the new SPECT analysis compared with planar analysis. Gastric volume postprandially exceeds the fasting volume plus meal volume. The course of volume change and gastric emptying differ over time. Higher differences in volumes exist relative to fasting plus residual meal volumes at 15 min (median 763 vs. 568 ml, respectively, \( P < 0.001 \)), 1 h (median 632 vs. 524 ml, \( P < 0.001 \)), and 2 h (median 518 vs. 428 ml, \( P < 0.02 \)), in contrast to similar volumes at 3 h (median 320 vs. 314 ml, \( P = 0.85 \)). Analysis of SPECT imaging accurately measures gastric emptying compared with planar imaging with median differences of 1% (IQR −2.25 to 2.0) at 1 h, 1% (−3.25 to 2.25) at 2 h, and −2.5% (−4 to 0) at 3 h. Gastric volume exceeds meal volume during the first 2 postprandial hours, and simultaneous measurements of gastric volume and emptying can be achieved with a novel 3D SPECT method.

THE GASTRIC BAROSTAT TECHNIQUE was the first method to accurately measure gastric relaxation after a meal, and it is generally regarded as the gold standard (1). However, the invasive nature of this procedure limits its use in clinical practice, and reproducibility data on the volume responses under pressure clamp are limited (21). There is also evidence that the intragastric balloon clamped at low continuous pressure perturbs gastric functions such as meal distribution and emptying (18, 19). Given the association of dyspepsia with either reduced accommodation or impaired (delayed or accelerated) emptying of the stomach, simultaneous measurement of these functions would be advantageous in clinical and research practice. The invasive nature of the barostat and perturbation of gastric emptying by space occupation within the stomach reduces its potential as an application to simultaneously measure volume or relaxation responses and emptying. Therefore, a noninvasive, comfortable yet sensitive, and reproducible alternative method is needed to assess the postprandial functions of the stomach.

Several imaging techniques [ultrasound (12), magnetic resonance imaging (15), single photon emission computed tomography (SPECT) (14)] and two nonimaging assessments [satiety drinking test (23), water load test (2, 13)] have been proposed. The overall performance characteristics of these methods have been reviewed elsewhere (11).

Our group has reported that SPECT provides gastric volume measurements that were well correlated with simultaneous barostat recordings (3). In a separate study that did not simultaneously appraise the measurement of volume responses by SPECT and by barostat, it was suggested that SPECT was inaccurate and merely reflected the volume of meal in the stomach (25). However, several pitfalls in the latter study have been identified (9), and the Temple group (22) confirmed the ability of SPECT measurements to quantify changes in gastric volume consistent with the accommodation of the stomach after standard meals, as previously reported by our group. Indeed, the same group incorporated the well-established methods to measure gastric emptying and concurrently measured gastric emptying and volume responses using separate SPECT and planar acquisitions (22). In the latter study, the three-dimensional (3D) imaging reconstruction algorithms for volume measurements were not validated with an independent gold standard.

The aims of the present study were to measure the relationship between the gastric volume response and emptying after a mixed, solid-liquid meal using 3D imaging, to assess the reliability of the 3D method to measure gastric emptying, and to describe the time course of changes in gastric volume during emptying of the meal in health. The latter aim was intended to explore the hypothesis proposed by van den Elzen et al. (25) that gastric volume measurements with SPECT merely reflect the volume of the meal in the stomach.

MATERIALS AND METHODS

Participants. We enrolled 20 female and 10 male healthy participants who were screened for gastrointestinal symptoms using a validated gastrointestinal symptom questionnaire. The average age was 31.6 ± 1.6 yr (±SE), weight was 72 ± 2.4 kg, and body mass index 25.1 ± 0.59 kg/m².

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The gastric volume after a solid meal in humans was measured using 

$^{99m}$Tc-SPECT to measure gastric volume. $^{99m}$Tc-sodium pertechnetate is known to be taken up by the gastric mucosa after intravenous administration (20). We have used this characteristic of $^{99m}$Tc-sodium pertechnetate to measure the gastric volume using SPECT (3, 15). Ten minutes after the intravenous injection of $^{99m}$Tc-sodium pertechnetate (10 mCi), dynamic tomographic acquisition of the gastric wall was performed using a dual-head gamma camera (SMV Fx-80 SPECT System, General Electric). For each SPECT acquisition, a total of 128 images was acquired over 360° at 5 s per image. After reconstruction of the transaxial images, a 3D rendering of the stomach and its volume was obtained using the Mayo Imaging Studio (MIS; Mayo Foundation, Rochester, MN) image-processing programs. This was accomplished by identifying the stomach in the transaxial SPECT images and separating the stomach from background using a semiautomated edge detection segmentation algorithm.

**Testing procedure.** Gastric emptying of solids was measured using the scintigraphic method that has been validated and reported previously (5, 8). Briefly, fasting volunteers presented to the research unit, and a blood pregnancy test was performed (when applicable) within 48 h of the test. $^{111}$In-labeled chloride (0.1 mCi) adsorbed to activated charcoal powder was added to two raw eggs during the scrambling, cooking process. The eggs were served on one slice of bran bread along with a 240-ml glass of skim milk (total calories: 302 kcal, 32% protein, 35% fat, 33% carbohydrate). The weight of the meal was 368 g.

Gastric emptying data were analyzed as in previous studies (5, 6, 8). Geometric mean of decay-corrected counts in anterior and posterior images of the stomach was used to estimate the proportion of $^{111}$In emptied at each time point (gastric emptying).

**Imaging procedure.** A dual-isotope procedure for simultaneous measurement of gastric accommodation (using $^{99m}$Tc) and gastric emptying (using the $^{111}$In-labeled meal) was developed with tomo- graphic acquisition over 360° on a dual-head gamma camera SPECT system. The SPECT acquisition is started at $-20°$ (340°) rather than the conventional $0°$. Images are acquired every $3°$ for $-5$ s per image. On completion of the study, the image data from $-20°$ to $+20°$ (12 images) are summed to give a composite anterior view of the stomach (Fig. 1). Similarly, the data from $160°$ to $200°$ are summed to provide a composite posterior view of the stomach. These two images are used for measurement of gastric emptying.

In 22 of the 30 healthy volunteers, additional anterior and posterior planar images were acquired at 1, 2, 3, and 4 h using the same camera in planar mode collecting 2-min anterior and posterior images for completion of the gastric emptying measurement. Both heads were positioned at the same distance from the subject’s body as determined by the body contour mapping process for the SPECT-imaging procedure.

Additional SPECT images (each lasting 15 min) were acquired preinjection of the meal and at several times up to 3 h postmeal ingestion to complete the gastric accommodation procedure. The times of SPECT images were fasting, 0, 15, 60, 120, and 180 min after the meal. The MIS software was used to (1) strip the required planar images from the tomographic data and integrate them into the gastric emptying study, (2) perform measurement of gastric accommodation, and (3) perform measurement of gastric emptying.

**Statistical analysis.** All data are presented as median, interquartile range, and 5–95 percentiles with individual outliers indicated as single data points (Fig. 2). We used ANOVA to compare sequential volumes of the stomach over time. Accuracy of gastric emptying measurements by 3D SPECT imaging was assessed by comparing the percentage emptied from the stomach at 2 h after the radiolabeled meal with the data from planar [2-dimensional (2D)] imaging. We also estimated the median and interquartile ranges of the differences in the proportion emptied from the stomach at 1, 2, and 3 h. Plots of summary data qualitatively compared the volume of the stomach and the proportion remaining in the stomach.

In addition, we estimated the intragastric volume by the product of the ingested meal volume (368 ml) multiplied by the median percentage of isotope remaining in the stomach at defined times; that is, at 15 min and 1, 2, and 3 h. This was used to estimate the difference between postprandial volume measured by SPECT and the sum of the fasting gastric volume (median 200 ml) plus residual meal at each time. For each individual, the SPECT-measured volumes and the estimated postprandial volume from actual gastric volume and percent residual of the meal were computed at 15 min and 1, 2, and 3 h. Within individual volumes at these times were compared by paired $t$-test. These differences were used to evaluate the relationship between the gastric volume and emptying at different stages in the postprandial period and to indirectly assess whether SPECT volume merely reflects the volume of the meal ingested, as suggested by others (25).

**RESULTS**

Gastric volumes during simultaneous measurements of volume and emptying. Gastric volume increases promptly to a maximum in the first 15 min after the meal. The median volume during the first 30 min after the meal is 787 ml, which is greater than the sum of the fasting volume (median 200 ml) plus the volume of the meal itself (368 ml). The gastric volume over the first two postprandial hours is significantly greater than the fasting gastric volume ($P < 0.05$ by nonparametric ANOVA and Dunn’s method, Fig. 2A). At 3 h, the median...
gastric volume was 320 ml, which was not significantly different from the fasting volume. Figure 2B shows the average change in volumes (postprandial minus fasting) after the meal and the volume ratio (fed volume/fasting volume) for all participants in the study. Note that, for all individuals, the change in volume during the first 30 min exceeds the volume of the meal.

Gastric emptying during simultaneous measurements of volume and emptying. Gastric emptying of the standard meal (Fig. 3) during measurements of gastric volume provided data that are in the range previously described using the same method when only gastric emptying was measured (5, 8).

Accuracy of gastric emptying measurements using SPECT. As indicated above, the gastric emptying measured by planar imaging was consistent with normal emptying. Accuracy of gastric emptying analysis of summed abstracted images by 3D SPECT acquisition was internally validated by measurements of the gastric emptying using the 2D (planar) imaging, which is the current gold standard. The Bland-Altman plot in Fig. 4 shows the data calculated by the 3D and 2D (planar) imaging using the same camera at 2 h. Note that the majority of values of gastric emptying at 2 h is within 5% error from the mean value, which approaches the zero line (or line of identity). Thus summed images collected by means of SPECT imaging accu-
Gastric emptying compared with planar imaging has a median difference of 1% (IQR = -2.25 to 2) at 1 h, 1% (-3.25 to 2.25) at 2 h, and 2.5% (-4 to 0) at 3 h.

**Time course of the relationship between gastric emptying and volumes.** Simultaneous measurements of gastric volume and emptying provide the opportunity to observe the time course of the two physiological processes simultaneously (Fig. 5). The time courses of the volume change and gastric emptying differ over time. Note in Fig. 6 that the process of emptying is associated with a reduction in gastric volume and that, despite the emptying of the meal (Fig. 5), there is still a large gastric volume. Thus, for example, there are high differences in measured volumes relative to fasting plus residual meal volumes at 15 min [median 763 vs. 568 ml (0% emptied), respectively]. Similarly, at 1 h, the median volume (632 ml) is greater than the sum of the median fasting volume (200 ml) and the estimated volume of meal remaining in the stomach (median 200 ml) plus the estimated volume of meal remaining in the stomach (median 88% of 368 or 324 ml). Later, however, the volume of the stomach tracks more closely the volume of the meal in the stomach. At 2 h, the median volume (518 ml) is close to the sum of the volume of the stomach during fasting (median 200 ml) plus the estimated volume of meal remaining in the stomach (median 62% of 368 or 228 ml) for a total of 428 ml. At 3 h, the median volume of 320 ml is close still to the sum of fasting volume (median 200 ml) plus the estimated meal volume (31% of 368 or 114 ml) for a total of 314 ml. The measured SPECT volumes and estimated gastric volumes (fasting plus estimated intragastric meal volume) are shown in Table 1. Note that SPECT volumes are significantly higher than estimated volumes at 15 min ($P = 0.001$) and 1 h ($P = 0.002$) and 2 h ($P = 0.02$), but not at 3 h ($P = 0.85$).

**DISCUSSION**

Our study shows that gastric volume measurements obtained during simultaneous measurements of gastric volume and emptying are in the range previously described using the same 3D method exclusively for estimating gastric volumes (3, 10, 15). Similarly, the novel measurement of gastric emptying using reconstruction of images obtained by the SPECT camera provides accurate measurement of gastric emptying. This has been demonstrated by Bland-Altman analysis (Fig. 4) and by direct comparison of calculated gastric volumes to SPECT measurements (Fig. 6). The latter shows that the difference in gastric emptying measured by SPECT is not only the volume of the meal plus fasting volume.
important practical implications for the investigation of the different gastric motor functions in health, disease, and pharmacodynamic studies. The ability to perform such simultaneous measurements reduces time required for investigation of these processes, which have previously been performed on separate days. In the future, it would be beneficial to validate this imaging technology to differentiate regional changes in volume and meal distribution within the stomach to further characterize regional physiology of the stomach.

Besides confirming the observation of feasibility by Simonian et al. (22), our current study also validates the critically important measurements of gastric emptying and gastric volume with the same SPECT camera and avoids the need to transfer the patient between two cameras for the measurements of gastric volume and emptying. This validation step is key before widespread application of the method. The Bland-Altman plot shows the remarkable accuracy of the SPECT-acquired gastric emptying data, and these data provide the basis for calculating coefficient of variation of primary endpoints of interest for future studies [e.g., gastric emptying at 2 and 4 h (24), fasting gastric volume, and postprandial change in gastric volume during the first 30 min].

The second important observation of these simultaneous studies is that we provide a clearer understanding of the relationship of gastric volume and intragastric content. These data suggest that the volume measured by SPECT far exceeds the volume of the meal ingested during the first 2 h postprandially. The time course of the gastric volume change reflects, in part, gastric emptying during the next 2.5 h. However, the measured gastric volume only returns to fasting volume plus meal volume at 3 h postprandially.

The difference in gastric volume versus fasting plus ingested volume observed particularly during the first postprandial hour is attributable to swallowed air during meal ingestion and more importantly to the gastric secretion (acid, pepsin, etc.) in this period. Thus Malagelada et al. (16) used classic physiological studies with intubation techniques and double marker dilution to measure volumes after meal ingestion. In these elegant studies, they demonstrated that during the first postprandial hour, there is a secretory volume output of 90 ml/10 min over baseline fasting values. They also observed an average gastric volume, after a 375-g solid-liquid meal, of ~420 ml during the first postprandial hour. The exponential emptying of the aqueous phase (240 ml of water in the meal and gastric acid secreted in response to the meal) presumably explains the difference between the estimated additional 540 ml/h and the average ~50 ml volume in excess of the ingested material measured during each 10 min of the first postprandial hour.

The current data acquired with SPECT are therefore consistent with the observations of gastric volume provided by intubated studies, because the latter showed that, by ~3 h after the meal, the gastric volume had returned to baseline (fasting) levels.

We acknowledge that the calculated difference in volume is a conservative estimate, because it assumes that the isotope labeled the entire intragastric meal, which is probably incorrect during the first 60 min postprandially while the solid radiolabeled food is being retained and triturated (17) and the unlabeled caloric liquid phase is emptying linearly or exponentially from the stomach (4, 7). Thus the intragastric volume is likely lower than the estimate provided, and this leads to the conclusion that SPECT-measured volumes do not merely measure the volume of the meal ingested but also the gastric volume output in response to the meal. Our data convincingly demonstrate that SPECT measurements are consistent with classic physiological measurements that required intubations.

We have previously validated the volume measurements in response to a meal and to gastric distension using the barostat balloon simultaneously as the gold standard (3). In the current study, we have validated the accuracy of the SPECT method for measuring gastric emptying using planar imaging as the gold standard. We conclude that simultaneous 3D SPECT assessment of gastric volume and emptying in response to a mixed meal provides measurements of the dynamic relationship of gastric volume and emptying in health.

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