Gastric Emptying Measurements: Delayed and Complex Emptying Patterns Without Appropriate Correction

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Anteriorly acquired and geometric mean corrected gastric emptying curves of solids and liquid isotopic-labeled meals were compared in 37 subjects given 61 meals of three different sizes. Anterior data alone consistently and significantly underestimated solid-phase gastric emptying rates with all meal sizes when compared to geometric mean acquired data. However, with liquids there were only slight differences between anterior and anterior and posterior geometric mean corrected emptying-rates. The difference probably reflects greater attenuation of the 140 kev photon of ^{99m}Tc compared to the 247 keV photon of ^{111}In. With anterior data alone, an apparent early delay in emptying of solids was present with all meal sizes and the resultant emptying curves were nonlinear in shape. Geometric mean correction resulted in the linearization of the solid-phase emptying curves and essentially eliminated the apparent delay in emptying or lag phase noted with the anterior data alone. Based on our results, geometric mean correction techniques are necessary for accurate assessment of radioisotopic-labeled solid meals.

J Nucl Med 26:1206–1210, 1985

Tothill et al., in 1978, documented that the measurement by rectilinear scanning techniques of transit of gastrically administered radionuclides was markedly influenced by the position of the detector probes and by the direction of the imaging (*1*). They found that anteriorly acquired counts alone, compared to anterior and posterior corrected geometric means, significantly underestimated gastric emptying rates for solid and liquid meals. Christian et al. later confirmed these findings employing gamma camera techniques (*2*). Yet, most of the reported studies on gastric emptying employing radionuclides are performed from the anterior view alone without any attempt to correct for the changing distribution of the radionuclide within the stomach and consequent alteration in marker attenuation (*3-8*). Several authors have also reported an apparent delay, or lag time in gastric emptying immediately following meal conclusion lasting for variable lengths of time (*3,9,10*). The purpose of this investigation is to evaluate the need for correction techniques in improving the accuracy of the measurement of gastric emptying rates. Specifically, we wish to examine the influence of geometric mean correction on the appearance of an early delay period in emptying and the effect of correction on curve shape.

Received Nov. 5, 1984; revision accepted June 25, 1985.

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MATERIALS AND METHODS

Subjects

A total of 37 subjects were studied. All had discontinued medications of any kind for three days prior to testing. They were not allowed to smoke during performance of the emptying study. Informed consent was obtained following approval by the Institutional Review Boards of the University of Utah and the Veterans Administration Medical Center and Development Committees.

Meals

After a 20-hr solid-food fast, each subject was given a standardized meal of 50, 300, or 900 g. The meals were of the following composition:

50 g. Twelve healthy male subjects (mean age = 31 ± 2.5 yr; range 23–51; mean weight = 76.9 ± 4.2 kg; range

54.5–104.5) were given 25 g of beef stew and 25 g of orange juice. Meal consumption time was less than 1 min.

300 g. Eight healthy male subjects (mean age = 31 ± 2.5 yr, range 23–51; mean weight = 80.9 ± 2.5 kg; range 72.2 – 95.5) were given 150 g of beef stew and 150 g of orange juice. Each was studied four times on different study days to yield a total of 32 studies. Meal consumption time was less than 5 min.

900 g. Seventeen healthy males (mean age = 31.5 ± 1.8 yr; range 24–51; mean weight = 78.4 ± 3.1 kg; range 53–107) were given 900 g meals consisting of 200 g of beef stew, 200 g of apple sauce, 50 g of bread, 225 g of whole milk and 225 g of orange juice. Meal consumption time was 10 min or less.

SOLID-PHASE MARKER

For each study, 5 mCi of technetium-99m- (^{99m}Tc) labeled sulfur colloid was injected into 20–50 g of canned liver patè (Sells) and fried until crisp. From 3–6 g of the fried patè (containing ~600 μCi of ^{99m}Tc) was mixed thoroughly with the beef stew prior to ingestion. The estimated radiation exposure to the 600 μCi dose of ^{99m}Tc is 11 mrad for the total body and 144 mrad for the stomach (*11*). Labeling efficiency and stability of the paté marker have been previously reported (*12*).

LIQUID-PHASE MARKER

One hundred microcuries of indium-111 (^{111}In) diethylenetriaminepentaacetic acid (DTPA) was mixed with the orange juice. In all studies, the labeled orange juice was consumed after the solid portion of the meal and immediately before the first gastric image. The estimated radiation exposure with this dose is 24 mrad for total body and 44 mrad for the stomach (*11*).

RADIOISOTOPIC COUNTING

Imaging techniques and validation studies have been reported (*2,12*). Images were obtained at 10–30 min intervals, depending on meal size beginning with the first image taken at meal conclusion (0 time). A 410 keV collimator was used. Solid and liquid phases of gastric emptying were recorded separately by setting the pulse-height analyzer on the 140-keV photopeak of ^{99m}Tc and the 247-keV photopeak of ^{111}In.

Subjects sat while eating and in between counting intervals and stood for abdominal imaging and 40–60 sec counts. A ^{99m}Tc point source was taped to the chest to allow accurate horizontal and vertical repositioning of the subject between images. The point source was marked on a persistence oscilloscope to reposition the subject. Images and counts were obtained at fixed timing intervals until greater than 50% of the solid marker had emptied. At every timing interval, images were acquired in the anterior and posterior projection. The 1-min interval between recording the anterior and posterior counts was not believed to introduce any significant error in the calculations. Technetium-99m counts were corrected for downscatter interference from ^{111}In by subtracting a measured downscatter fraction of the ^{111}In counts from the ^{99m}Tc counts. The ^{99m}Tc data were corrected for radioactive decay. The geometric mean of the anterior and posterior counts (the square root of the product) was calculated. Background correction was not performed since the orally ingested radiotracer does not measurably leave the GI tract during the course of the study. The counts observed at each imaging interval were normalized to a percentage of the counts obtained at the first image (0 time), which was assigned a 100% value. The results were expressed as the percent of retention at each imaging time for both the solid and liquid markers. The emptying half-times ($t_{1/2}$: the time when 50% of the marker had emptied) were computed by interpolation from the observed data.

STATISTICAL ANALYSIS

The means of the percent retention values and the $t_{1/2}$ values for the anterior alone and geometric mean data were compared at the corresponding timing intervals for both markers. Paired two-tailed Students t-tests of significance were employed.

RESULTS

Solid-phase emptying

Figure 1, upper panel, shows the mean retention values for the anterior and geometric mean corrected curves for all three meal sizes.

50 g meals: The mean percent retention values of the anteriorly acquired data were significantly ($p < 0.01$) higher than the geometric mean values at all timing intervals. The observed mean $t_{1/2}$ value was also significantly ($p < 0.01$) higher (anterior mean $T_{1/2} = 41.5 \pm 5.4$ min, geometric mean $T_{1/2} = 35.9 \pm 5.3$ min).

300 g meals: The mean percent retention values of the anteriorly acquired data were significantly ($p < 0.001$) higher than the geometric mean values at the 20-, 40-, 60-, and 80-min intervals. The observed mean $T_{1/2}$ value was also significantly ($p < 0.001$) higher (anterior mean $t_{1/2} = 83.4 \pm 3.5$ min; geometric mean mean $T_{1/2} = 60.3 \pm 4.4$ min).

900 g meals: The mean percent retention values of the anteriorly acquired data was significantly ($p < 0.01$) higher at all timing intervals. The observed mean $T_{1/2}$ value was longer for the anterior data alone but it was not significantly different (anterior mean $T_{1/2} = 115.1 \pm 9.3$ min; geometric mean $t_{1/2} = 108.8 \pm 8.1$ min).

Inspection of the anteriorly acquired emptying curves in Figure 1 reveals an early delay in emptying with all three meal sizes and is particularly marked for the 300 g meal in which an actual increase in counts was observed at the 20-min interval. The geometric mean corrected curves, in contrast, reveal no apparent early delay in emptying with any meal size and the linearization of the emptying curves.

Liquid-phase emptying

Figure 1, lower panel, shows the mean percent retention values for the anterior and geometric mean corrected curves for all three meal sizes.

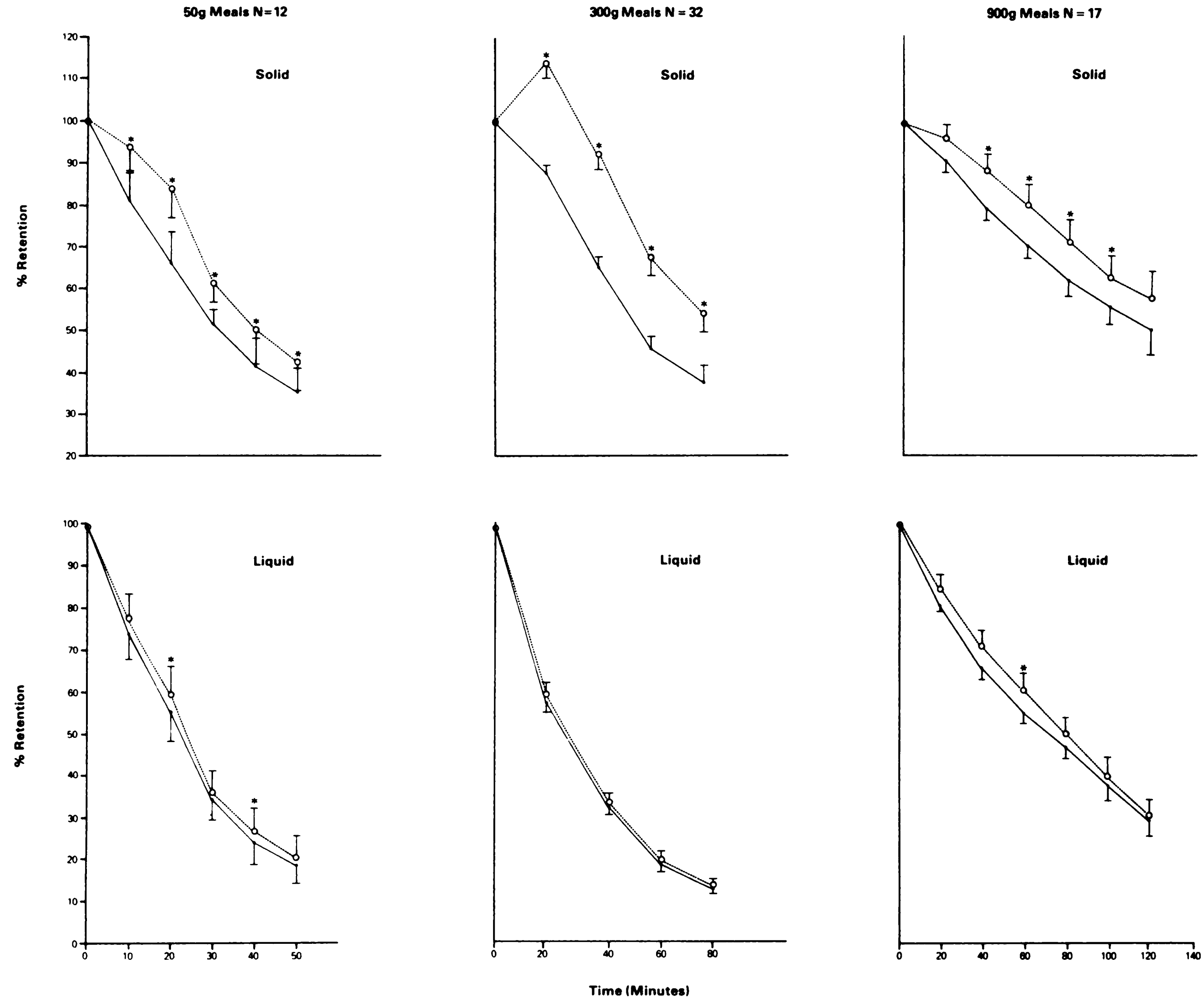

FIGURE 1
Mean percent retention values ± s.e.m. for solid (upper panel) and liquid (lower panel) labeled phases. Anteriorly acquired values (O- - -O) are compared to geometric mean-corrected values (●- - -●) at all timing intervals. Asterisks represent statistically significant differences at the indicated timing intervals by paired t-test analysis (see text for values)

50 g meals: The mean percent retention values of the anteriorly acquired data were significantly ($p < 0.05$) higher only at the 20- and 40-min timing intervals. The observed $t_{1/2}$ was also slightly but significantly ($p < 0.05 > 0.02$) higher (anterior mean $T_{1/2} = 25.2 \pm 2.4$ min, mean geometric mean $t_{1/2} = 23.9 \pm 3.6$ min).

300 g meals: The mean percent retention values for the anterior and geometric mean data did not significantly differ at any timing interval. The mean $T_{1/2}$ values were also not significantly different (anterior mean $T_{1/2} = 26.1 = 1.8$ min; geometric mean mean $T_{1/2} = 25.1 \pm 1.4$ min).

900 g meals: The anteriorly acquired mean percent retention values were significantly ($p < 0.05$) higher than the mean geometric mean values at the 60-min timing interval only. The observed mean $T_{1/2}$ values were not significantly different (anterior mean $T_{1/2} = 77.0 \pm 6.3$ min; mean geometric mean $T_{1/2} = 74.0 \pm 5.6$ min; $p > 0.05$).

The liquid curves do not demonstrate a delay in early emptying and show no significant difference between the anterior and the geometric mean corrected curves. The anterior image curves were slightly higher for all three meal sizes.

DISCUSSION

These findings support the original observations of Tothill et al., and expand those of Christian et al. who documented substantial inaccuracies in solid and liquid meal radioisotopic counting measurements when reliance was placed on measurements from a single detecting position (*1,2*). Both groups reported underestimation of solid phase emptying rates when anterior detection alone was used as compared to when bilateral anterior and posterior correction was used. Other groups, employing correction measurement techniques, have noted the same inaccuracies with single view imaging (*9,10,13,14*). The apparent explanation for the increase in anteriorly acquired counts is due to shifting

TABLE 1
Solid-Phase Emptying Half-Time ± s.e.m.

Meal size (g)	N	Time (min) Geometric mean data	Time (min) Anterior data	Average percent difference	Extreme* percent difference
50	12	35.9 ± 5.0	41.5 ±5.4	15.6	50.0
300	32	60.3 ± 3.5	83.4 ± 4.3	38.1	86.8
900†	15	108.8 ± 8.1	115.1 ± 9.3	5.7	39.1

† Excluding two of 17 studies because of extremely prolonged extrapolated anteriorly acquired emptying-half times (in excess of 400 min).
* In single study within series.

of the labeled solid food mass from a posterior to a more anterior position in the stomach and towards the anterior detector during meal digestion. In phantom studies, in which the position of the labeled food mass within the stomach was simulated, a shift of as little as 2.54 cm caused a 35% increase in the anterior count (*2*). In these same studies, geometric mean correction provided a point-source sensitivity for ^{99m}Tc of ±1.9% for depths between 5 and 20 cm and ±3.3% below 2.54 cm and above 22.86 cm. These data are in agreement with similar studies by Ferrant and Cauwe (*15*), using the geometric mean technique. The measurement requires two detectors positioned anteriorly and posteriorly, as employed by Tothill et al., or may be obtained with a single gamma camera with the subject alternately rotating to an anterior and posterior position at each counting interval as was done in this study.

It is apparent from Fig. 1 and Tables 1 and 2 that the error in anterior measurement alone is consistently large for solid-phase emptying, particularly with the smaller meal sizes, while the error produced in liquid phase emptying is much smaller and apparent only with the 50 and 900 g meal sizes. The effect of the geometric mean correction on liquid emptying is less significant for two reasons: (a) the 247-keV gamma photon of ^{111}In has a smaller attenuation coefficient in tissue; and (b) the liquid marker empties at a faster rate than the solid marker.

An early delay, or "lag" phase, in gastric emptying in healthy subjects has been reported by several groups (*3, 9, 10*). The anteriorly acquired emptying curves in Fig. 1 clearly show a delay in early emptying for all solid-phase ^{99m}Tc meals compared to the geometric mean corrected data; this delay is most apparent with the 300 g meal in which an actual increase in retention of the marker was recorded at the 20-min counting interval. The apparent early delayed period of emptying all but disappeared with geometric mean correction producing a linear emptying curve with all three meal sizes. These observations are pertinent to the application of curve-fitting formulas to grouped data. Recommendations for complex curve-fitting formulae have been made by at least three groups of investigators who did not employ geometric mean correction (*16–18*). Their nonlinear, curve-fitting formulae were based, in part, on the recognition of a consistently observed early delay in solid-phase emptying. With geometric mean corrected data in three reported studies performed on healthy subjects, the emptying curves for the groups most closely conformed to a linear fit, without evidence of a delayed early phase of emptying (*1, 13, 19*). However, even with corrections, early delayed phases in emptying in groups of healthy subjects are described for which more complex curve fitting formulae may be appropriate (*9, 10*). We are unable to explain these discrepancies in grouped data but suggest that differences between studies in subject selection, meal weight and composition or meal timing and counting intervals may account for a part of it.

TABLE 2
Liquid-Phase Emptying Half-Time ± s.e.m.

Meal size (g)	N	Time (min) Geometric mean data	Time (min) Anterior data	Average percent difference	Extreme percent difference
50	12	23.9 ± 3.6	25.2 ± 4.0	5.5	20.0
300	32	25.1 ± 1.4	26.1 ± 1.8	4.0	65.6
900	17	74.0 ± 5.6	77.0 ± 6.3	4.1	25.0

In conclusion, gastric emptying studies of three meal sizes in 37 healthy subjects has shown that appropriate correction techniques are necessary to accurately measure solid-phase gastric emptying rates. With the higher gamma-ray energy liquid-phase marker emptying, however, these corrections are probably not necessary (*14, 18*). The failure to employ correction techniques in solid-phase emptying curves has resulted, in some studies, in an apparent early delay period in emptying and in misleading nonlinear emptying curves. We do not conclude that such an early emptying delay period does or does not exist but rather that an apparent early emptying delay can be artifactually created by not employing appropriate correction techniques. We do not suggest that previous solid emptying studies employing anterior data alone are invalidated thereby. Provided the limitations of anterior detection alone are appreciated unilateral measurements will suffice for most clinical studies where gross differences in emptying rates between groups of subjects are sought (*3, 4, 8*).

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