Comparison of Left Anterior Oblique and Geometric Mean Gastric Emptying

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A left anterior oblique image (LAO) and the geometric mean of anterior and posterior counts have both been proposed as methods for acquiring gastric emptying data. Both approaches are used to correct for the changes in attenuation that occur as the depth of radiolabeled solids changes during gastric emptying. These two methods were compared by using a power exponential curve fit to calculate a lag phase, an equilibrium emptying rate, and a half-time for gastric emptying in 20 patients. There were no significant differences (mean ± 1 s.e.m.) in the measured half-emptying time (115 ± 10 versus 104 ± 7 min) (p = 0.08) or rate of gastric emptying (0.015 ± 0.002 versus 0.015 ± 0.002 min⁻¹) (p = 0.56) for LAO imaging versus the geometric mean. However, the LAO measurements of the lag phase were significantly higher (69 ± 7 min) than the geometric mean (53 ± 6 min) measurements (p = 0.004). This resulted in 4/20 (20%) of patients with normal geometric mean lag phase measurements who would have been reclassified as abnormal using the LAO method.

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Studies first by Cannon in animals (*1,2*), and later by others (*3*), have established the biphasic nature of gastric emptying of solid food. Noninvasive scintigraphic studies in humans have confirmed the presence of an initial preparatory lag phase followed by an emptying phase during which the stomach expels solids at a characteristic rate (*4–12*). As our understanding of the physiology of normal and abnormal gastric emptying improves, it is clear that scintigraphic studies should be analyzed in a manner which permits better characterization of this complex process.

Many scintigraphic studies have used the time to 50% emptying of solids or half-emptying time (T½) as an index of gastric emptying (*13–15*). Others have used a percent emptying measured at a fixed time (*16*). While both approaches have become common in clinical practice they do not fully characterize the biphasic nature of gastric emptying.

In order to accurately measure the lag phase, correction must be made for the changes in attenuation that occur as solids move from the posteriorly located fundus to the more anterior antrum. Several methods to correct for this have been proposed including the use of: a lateral view (*6*), peak-to-scatter ratio (*17,18*), and geometric mean analysis (*14,19*).

Most recently left anterior oblique (LAO) imaging of the stomach has been proposed based on the assumption that an imaging plane in which the food moves parallel to the face of the gamma camera will minimize changes in attenuation. The only study to validate such an approach, however, used a single measure of the percent of emptying at 60 min and did not include analysis of the possible effects on measurement of the lag phase or rate of gastric emptying (*18*).

The purpose of this study was to compare the results obtained by using an LAO acquisition with geometric mean analysis of gastric emptying data.

METHODS

This prospective study analyzed the results of gastric emptying studies on 25 successive patients referred because of symptoms suggestive of delayed gastric emptying. There were 10 males and 15 females aged 25 to 83 with a mean age of 53. The patient results were compared to 14 normal controls. Any patient gastric emptying parameter was considered abnormal if it exceeded 2 s.d.s of our previously published normal geometric mean values (mean±1 s.d.): k = 0.0142 ± 0.0034 min^{-1}, TLAG = 31.0±7.5 min, and T½ = 77.6 ± 11.2 min (*11*).

After an overnight fast, the patients ingested a standardized test meal prepared by mixing 500 μCi of ^{99m}Tc-sulfur colloid with two beaten, raw eggs. The eggs were then cooked until firm and placed between 2 slices of toasted white bread. The meal has a caloric content of 270 calories with 23% protein, 40% fat, and 37% carbohydrate. All patients were instructed to finish eating the meal within 7 min, following which they drank 300 ml of plain tap water.

Immediately after consuming the meal, the subjects were imaged standing upright in front of a large field of view gamma camera fitted with a low-energy, all-purpose collimator. Time zero (t = 0) was taken as the time at which the first set of images began. Sequential anterior, posterior, and LAO 60-sec images

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were acquired using a 128 × 128 byte mode matrix and nuclear medicine computer (NucLear MAC, Scientific Imaging, Denver, CO). The best LAO projection was determined by obtaining the largest diagonal dimension of the stomach on the persistence scope. All data were acquired using a 140 keV photopeak and 20% window. Images were acquired every 10–15 min for a minimum of 120 min. Between images the subjects were allowed to sit or walk about without restriction.

A manual region of interest corresponding to the gastric outline was determined for all images (Fig. 1). After correcting for decay, the percent of gastric activity was normalized to 100% for maximum gastric counts after ingestion of the meal. The percent of maximum gastric activity was calculated for all times for the LAO and the geometric mean (anterior counts × posterior counts)$^{1/2}$) counts. These data were then plotted and fit to a modified power exponential function:

$$y(t) = 100\ [1\text{-}(1\text{-}\exp(\text{-}kt))^{\beta}]$$

which has been previously shown to fit biphasic gastric emptying curves (*11*).

In this equation, y(t) is the percent of gastric activity at time t; k is the slope of the exponential terminal portion of the gastric emptying curve in $(\text{min})^{(-1)}$; and β is the extrapolated y intercept from the curve fit to the terminal portion of the emptying curve (Fig. 2). For solids, the initial delay in the onset of gastric emptying is characterized by a lag phase, TLAG, which is numerically equal in minutes to $\ln\beta/k$. This time corresponds to the inflection point of the gastric emptying curve where the second derivative of the function is equal to zero (*10,11*) and also corresponds to the time-to-peak activity in the distal stomach (*10*) (Fig. 3).

Analysis of the LAO and geometric mean data were performed using a non-linear, least squares regression according to the method of Levenberg and Marquardt (*20*) using a commercially available software program (LabVIEW 2.1, National Instruments, Austin, TX). The measure of the goodness of the fit for each curve was given by the mean squared error.

The T½ was calculated as the time to 50% emptying from the fitted curves.

The statistical comparisons of the LAO and geometric mean results were performed using a Student's paired t-test (STATVIEW 512+, BrainPower Inc., Calabasas, CA). Results were considered to be significant for $p \leq 0.05$.

RESULTS

Table 1 summarizes the data for k, TLAG, and the T½ values obtained for all patients for the geometric mean and LAO methods of analysis. There were five patients (#9, #17, #20, #23, and #25) with severe gastroparesis and almost no gastric emptying (<10%) in images obtained up to 150 min. Since no T½ or TLAG values could be calculated for these patients, they were excluded from the statistical analysis.

In all cases, except for the five excluded because of severe gastroparesis, the automated curve fitting program was able to fit the gastric emptying data. The mean values of the mean squared error for the LAO and geometric mean curve fits were 10.9 (range 1.9–24.8) and 16.6 (range 0.84–48.6), respectively.

For the 20 patients included in the statistical analysis, there was no significant difference (LAO versus geometric mean ± 1 s.e.m.) in the determination of k (0.015±0.002 vs 0.015 ± 0.002 min^{-1}) (p = 0.56). While the LAO T½

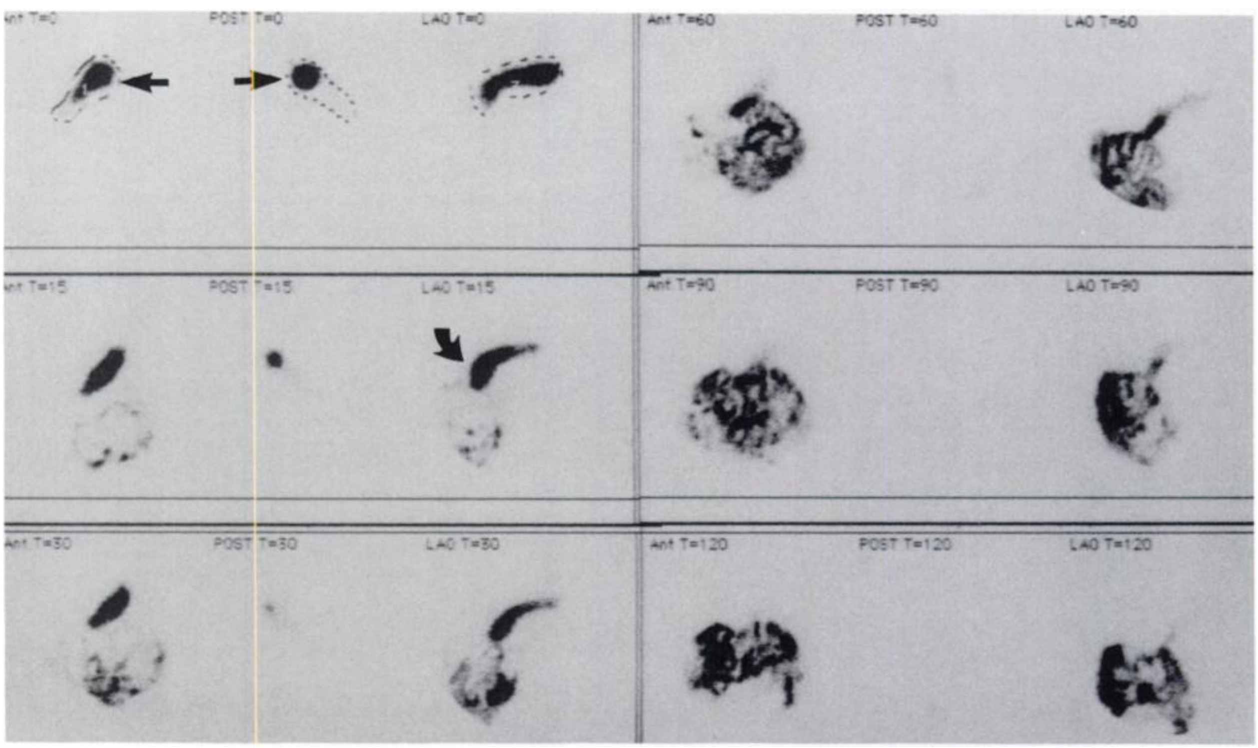

FIGURE 1. Normal study. Anterior, posterior and LAO gastric images are shown with examples of the regions of interest. In the earliest images (t = 0, 15 min), the solids are preferentially stored in the fundus. Fundal activity is most apparent in the anterior and posterior images (straight arrows). By 15 min, the solids have redistributed to the distal stomach (curved arrow).

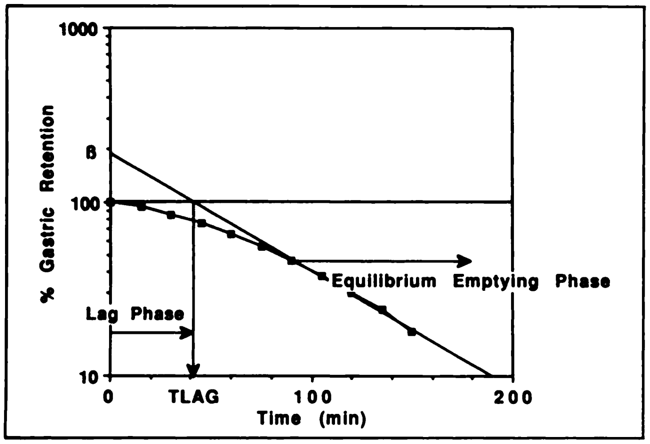

FIGURE 2. Biphasic gastric emptying. This graph illustrates how the power exponential function can be used to characterize the early lag phase and equilibrium emptying rate of a typical solid gastric emptying curve. The graph is a semi-logarithmic plot to demonstrate the linear fit to the terminal portion of the curve used to characterize the equilibrium emptying rate, k and its relationship to the y intercept, β, at t = 0.

TABLE 1
Gastric Emptying Data

Patient no.	K-GM	K-LAO	TLAG-GM	TLAG-LAO	T½-GM	T½-LAO
1	0.0134	0.0137	82	71	118	112
2	0.0264	0.0279	61	68	88	88
3	0.0133	0.0149	52	99	90	127
4	0.0115	0.0121	33	45	102	113
5	0.0112	0.0177	95	96	135	114
6	0.0035	0.0048	0	0	124	125
7	0.0049	0.0047	40	115	172	255
8	0.0452	0.0446	30	29	40	40
9	<0.005	<0.005	—	—	>150	>150
10	0.0132	0.0187	68	67	110	90
11	0.0092	0.0105	64	108	120	145
12	0.0125	0.0150	81	97	120	122
13	0.0066	0.0029	0	0	91	141
14	0.0243	0.0161	72	59	88	87
15	0.0183	0.0098	22	58	54	112
16	0.0086	0.0096	33	72	110	130
17	<0.005	<0.005	—	—	>150	>150
18	0.0157	0.0149	66	61	94	92
19	0.0084	0.0134	52	67	115	95
20	<0.005	<0.005	—	—	>150	>150
21	0.0168	0.0173	31	55	65	55
22	0.0167	0.0199	77	92	105	111
23	<0.005	<0.005	—	—	>150	>150
24	0.0111	0.0124	94	121	134	149
25	<0.005	<0.005	—	—	>150	>150

measurements tended to be longer (115 ± 10 versus 104 ± 7 min) this did not reach statistical significance (p = 0.08). However, measurement of TLAG (69 ± 7 versus 53 ± 6 min) was significantly longer (p = 0.004) by the LAO method. The increase in T½ in all cases appeared to be due to a shift of the LAO gastric emptying curves to the right (Fig. 4).

For clinical purposes in our laboratory, patients historically have been judged using geometric mean analysis to have abnormal gastric emptying based upon a T½ of greater than 100 min (e.g., > mean + 2 s.d. above our normal controls). There was agreement in the classification of 16 patients as having either normal (≤ mean + 2 s.d. of controls) or abnormal (> mean + 2 s.d. of controls) TLAG times. However, 4/20 (20%) judged normal using geometric mean analysis would have been reclassified as abnormal using the LAO method. Of these four patients, only one (#15) would have been reclassified as abnormal using T½ criteria. There was agreement in all cases between the LAO

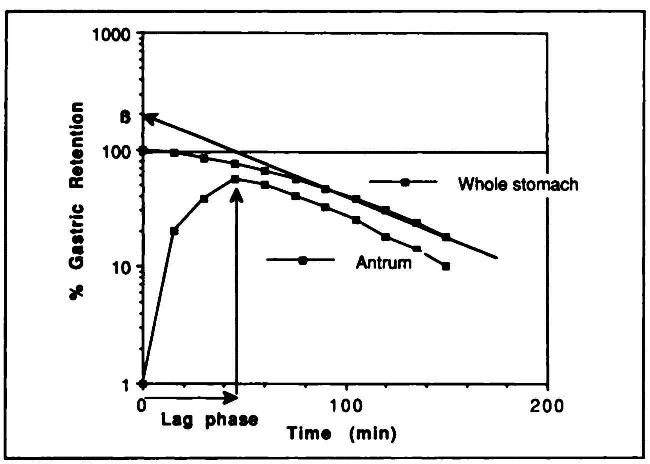

FIGURE 3. Antrum versus whole stomach gastric emptying curves. The lag phase measured by the power exponential is best illustrated by separately plotting the distal stomach (antrum) emptying compared to the whole stomach [modified from (*10*)]. As shown, the lag phase corresponds to the peak in distal stomach activity just prior to the onset of emptying of solids from the antrum. This corresponds to the inflection point of the fitted curve.

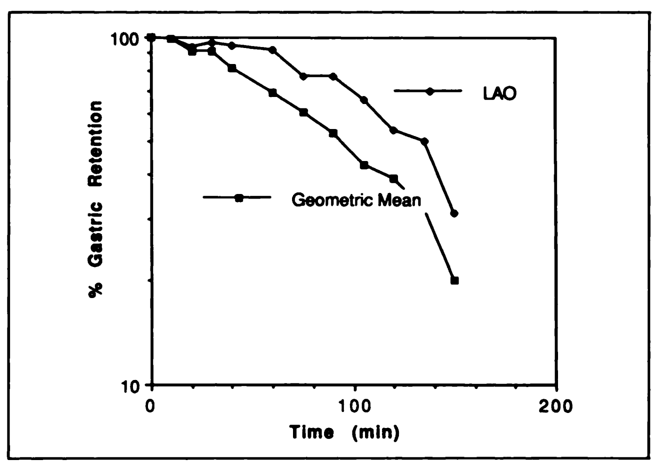

FIGURE 4. Geometric mean versus LAO Gastric Emptying. This example of the raw data (Patient 3, Table 1) demonstrates the typical shift of the LAO curve to the right which increases the measured T½. This is likely due to increasing counts not fully corrected by the LAO view during fundal-antral redistribution of solids during the lag phase.

and geometric mean analysis of the rate of gastric emptying.

DISCUSSION

Cannon first proposed that the fundus (proximal) and antrum (distal) portions of the stomach play separate roles in emptying of liquids and solids (*1*). Cannon observed that the fundus acts as a gastric reservoir which undergoes initial receptive relaxation to receive food from the esophagus (*2*). Solid foods are temporarily stored in the fundus until slow sustained contractions gradually transfer the food to the antrum. Once in the antrum, peristaltic contractions work by a process termed trituration to mix the solids with gastric juices and grind the solids to particles of 1-2 mm in size before they are permitted to pass through the pylorus (*9,21*).

Liquids, requiring no trituration, pass immediately following ingestion from the fundus to the antrum and promptly leave the stomach under control of a sustained pressure gradient generated by the fundus (*3*). Liquid emptying is monoexponential and in contrast to solids can adequately be described by a simple T½ value (*22*). Studies have shown that measurement of the rate of liquid emptying from the stomach requires less attenuation correction (*5,12*). While some have attributed this to the higher energy of the ^{111}In (247 keV) label used for liquids compared to the ^{99m}Tc (140 keV) label used for solids, it is likely that the rapid and uniform distribution of liquids throughout the stomach results in proportionately less anterior motion such as occurs with solids. Analysis of liquid gastric emptying is simplified however liquid emptying in the absence of solids is of little clinical use since it usually does not become abnormal until gastroparesis is far advanced (*8*).

Numerous scintigraphic studies have confirmed the biphasic nature of solid food gastric emptying (*6,8,9,11,23*). This has led to proposals for biphasic analyses of gastric emptying data (*24*).

In contrast to liquids, studies of solid food gastric emptying have demonstrated the need for attenuation correction particularly for characterizing the lag phase (*6,14,18,23,25*). Some authors have used a linear model to characterize the late phase following trituration which is characterized by an equilibrium emptying rate (*6,8*). We and others have found the rate to be non-linear (*11,24*).

The results of this study confirm that the method used to perform attenuation correction will affect lag phase measurements. Our finding that the LAO view yielded significantly longer times for the lag phase suggests that use of this single imaging plane does not completely correct for the posterior-anterior shift of solids from the fundus to antrum. The shift to the right of the LAO curves (Fig. 4) most likely is due to the apparent increase in detected counts that occurs with this movement.

There is commonly some overlap of the proximal duodenum with the distal stomach. This may increase gastric counts and result in an increase in the measured lag phase. Such overlap however occurs in the anterior as well as the LAO images and would not appear therefore to cause a selective affect on the LAO measurement of the lag phase.

Our finding that the emptying rate, k, calculated from the modified power exponential fit to the gastric emptying curve is independent of attenuation correction confirms previous studies showing that once solids have been triturated and are suspended with liquids, both empty at the same rate (*11,25*). This has led Siegel et al. to suggest that labeling of the solid component of the meal may be unnecessary, since k can be measured using a liquid label in the presence of unlabeled solids (*26*). Such characterization of k using the power exponential method has been shown to be useful for detecting early diabetic gastroparesis particularly in asymptomatic patients with cardiac autonomic neuropathy (*27*).

We used the geometric mean method for comparison in this study since it has been well validated and widely accepted as a "gold standard" (*6,12,14,19*). Phantom studies have shown a 3%–4% maximum variation in counts over depths typically encountered in gastric emptying studies (*11*). The major disadvantage associated with the geometric mean is the need to acquire two views. This makes dynamic imaging at a rapid frame rate impossible without a dual-headed gamma camera. For this reason, Fahey et al. (*18*) proposed use of the LAO view.

Compared to the rapidity of liquid gastric emptying, however, measurements of the early and late phases of solid emptying do not require continuous dynamic imaging. As defined in this study, they can be easily characterized using anterior and posterior images every 10–15 min and curve fitting with the modified power exponential function.

Since gastric emptying studies typically take up to 2–3 hr and require analysis of multiple images, the simplicity of the LAO approach is attractive. Fahey et al. performed a limited analysis of the LAO method comparing only the percent of gastric emptying at 60 min to the geometric mean. They did not define a lag phase stating that "the best parameter for characterizing lag phase remains to be seen" (*18*).

A definition and proper mathematical expression for the lag phase remains controversial. Some authors have chosen to define the lag phase visually "as the part of the solid-emptying curve prior to the appearance of detectable amounts of radiolabel of the solid phase in the proximal small intestine" (*4*). We have chosen to define it mathematically to reduce observer bias.

The measurement of the lag phase used in this study is based upon our previous work using a modification of the power exponential function first proposed by Elashoff et al. (*24,28*). This modified power exponential provides biphasic characterization of gastric emptying and can detect lag phase differences due to food particle size or the physical characteristics of different solids (*10,11*). In addition, these studies have demonstrated that it is important to analyze the proximal and distal stomach separately. With such analysis, TLAG corresponds to the time of peak filling of the distal stomach and the inflection point of the curve (Fig. 3). This is obtained mathematically by setting the second derivative equal to zero. Using this definition, the lag phase includes time for both the redistribution of solids from the fundus to the antrum as well as trituration. It ends after trituration is adequate so that solid particles can begin to empty from the antrum at a uniform rate.

While there is controversy on the best method to characterize the lag phase, there is no debate as to its physiologic meaning and clinical relevance. Collins et al. have stated that "the accurate measurement of the lag period is of importance in both clinical and physiologic studies of gastric emptying" (*23*). It appears to be a sensitive indicator of drug interventions employed to treat gastroparesis (*29*). Analysis of the lag phase has also been shown to be important to elucidate the effects of ulcer surgery on gastric emptying. Mayer et al. showed that there was obliteration of the lag phase following truncal vagotomy and pyloroplasty without an effect on trituration (*28*).

We conclude that use of an LAO method for acquisition and processing of gastric emptying data can result in significant overestimation of the lag phase compared to geometric mean analysis. The measurement of the equilibrium emptying rate is independent of the method for attenuation correction. While the LAO T½ measurements tended to be longer, they were not significantly different from geometric mean measurements for this group of patients. This study emphasizes the importance of performing biphasic analysis of gastric emptying using a mathematical model such as the power exponential fit, particularly, if one is to properly characterize lag phase abnormalities.

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