
Gastric Emptying Rate Assessment Based on the Proportion of Intra-Abdominal Radioactivity in the Stomach

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Using scintigraphic techniques, the rate of gastric emptying is calculated by quantifying the absolute radioactivity within a gastric region of interest (intra-gastric method) with the time of meal completion considered 100% retention. However, this technique has significant limitations arising from subject movement and radionuclide gamma-ray attenuation, which may render curve fitting difficult, particularly in patients with gastroparesis. In an attempt to minimize these limitations, we have expressed the intra-gastric content as a percentage of the total abdominal radioactivity (abdominal method) and compared these two methods. **Methods:** Forty-five subjects in a sitting position consumed a meal consisting of two fried eggs labeled with ^{99m}Tc , two slices of toast and 300 mL 5% glucose water (412 kcal). Data were acquired at a rate of one frame every 5 min from the left anterior oblique view. Using the two methods, the intra-gastric retention ratios at 30, 60, 90, 120 and 240 min and the 50% emptying time (T50) were obtained from both observation and calculation by power exponential fit. R^2 , representing goodness of fit of the nonlinear curve fitting, was calculated. **Results:** There were no differences in the calculated values of T50 between the two methods. Quantitative estimates of T50 by extrapolation of a power exponential fit were feasible in 42 of the 45 subjects when the abdominal method was used, compared with only 29 of the 45 subjects when the intra-gastric method was used. In the 23 subjects with delayed emptying, quantitative estimates of T50 were feasible in 20 subjects when the abdominal method was used, compared with 7 subjects when the intra-gastric method was used. Using the abdominal method as opposed to the intra-gastric method also significantly improved R^2 . The difference between observed values and estimated values of T50 and intra-gastric retention ratios at 30, 90 and 120 min was smaller using the abdominal method. **Conclusion:** Scintigraphic measurement of gastric emptying calculated using the proportion of the abdominal radioactivity in the stomach offers substantial advantages over conventional methods, particularly in patients with gastroparesis.

Key Words: intra-abdominal radioactivity; gastric emptying; scintigraphy

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Radionuclide studies remain the gold standard for evaluating gastric emptying in both research and clinical settings (1). For liquids, most investigators use the half emptying time (T50) as an index of gastric emptying (2–4). For solids, some investigators use T50, whereas others use the percentage emptying measured at a fixed time (2–5), because in some patients with delayed gastric emptying, the pattern of emptying is too irregular for accurate determination of the emptying curve and T50 (5–10). There are two possible causes for fluctuation of the curve: (a) Changes in attenuation occur as solids move from the more posterior fundus to the more anterior antrum (11–14) and (b) subject movement leads to changes in the spatial relationship between the collimator and the stomach (15). Conventionally, investigators have quantified the absolute radioisotopic counts within a gastric region of interest assuming a 100% retention at time 0 and expressed the counts as the percentage of retention at each imaging time. We assume that this technique neglects the postgastric radioactivity in the emptying process and is too dependent on intra-gastric counts that may elevate either in the lag phase, during which no emptying occurs, or in the postlag emptying phase, during which small intestinal radioactivity also elevates simultaneously, and therefore may account for fluctuation of the emptying curve.

In this study, we hypothesized that the expression of intra-gastric counts as a proportion of the total abdominal radioactivity would minimize technical errors, smooth the emptying curve and increase the feasibility of quantifying T50 by mathematical fitting simultaneously in the solid phase gastric emptying curve.

MATERIALS AND METHODS

Subjects and Groups

Forty-five subjects were enrolled in this study. So that the three groups would be diversified to fit different clinical emptying situations, the groups consisted of 10 healthy volunteers (6 men, 4 women; age range 21–55 y), 21 subjects with nonulcer dyspepsia (12 males, 9 females; age range 17–48 y) and 14 diabetic patients with chronic symptoms suggestive of gastroparesis (6 men, 8 women; age range 25–52 y). All subjects, except the healthy

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volunteers, underwent upper gastrointestinal endoscopy and abdominal sonography to rule out any organic diseases.

Data Acquisition

After an overnight fast, each subject ingested a standard mixed solid and liquid meal comprised two fried eggs labeled with 18.5 MBq (500 μ Ci) radioactive 99m Tc phytate (16), two slices of toast and 300 mL 5% glucose water (412 kcal). It was suggested that the meal be consumed within 5 min. After the meal, the subject was positioned sitting semiupright (approximately 60°) with pillows placed behind the head and under the knees to maximize comfort and minimize subject movement. Two markers (1.5-cm diameter, lead-lined, plastic bottle tops containing cotton wool soaked with 0.2 MBq [5 μ Ci] radioactive 99m Tc phytate) were fixed to the skin. One was situated in the right hypochondrium at the end of the ninth rib and the other over the left anterosuperior iliac spine (17). These remained in position throughout the procedure to establish anatomic reference points, which were used to correct for subject movement during the procedure. A large-field-of-view gamma camera (Elscont ECT 609R; Elscint Ltd., Haifa, Israel) with a medium-energy collimator was positioned in the 45° left anterior oblique (LAO) view (8) and at a distance of approximately 10 cm so that the whole abdominal cavity could be monitored. At 5-min intervals, the camera captured frames and transmitted them to a computer for analysis and storage. This process took 60 s for each frame. The data were collected as follows: Of the 45 subjects, 24 underwent the minimum testing period of 90 min, and the other 21 (14 patients who had nonulcer dyspepsia and 7 who had diabetes and suspected gastroparesis) underwent an expanded 240-min regimen, during which we obtained T50 observation values for comparison with the mathematical estimation values. These 21 subjects were allowed to use the toilet midway through the experiment, after 120 min of testing. The completed study was reviewed in cine mode to check for patient movement. When significant movement was detected, the images were realigned using the double radioisotope markers as reference points.

Data Analysis

Time 0 was considered the time of meal completion. The retention of the meal in the stomach was defined as 100% at time 0. The lag phase was defined as the time elapsing before the appearance of any isotopes in the small intestine (18). The intragastric method for plotting the decay-corrected time-activity curves used absolute intragastric counts expressed in terms of 100% retention at time 0. The abdominal method, using the proportion of intra-abdominal radioactivity in the stomach at each imaging time, was expressed as intragastric counts divided by intra-abdominal counts. Therefore, the proportion of the meal remaining in the stomach before any radioactivity reached the small intestine was considered 100%, regardless of the variation in intragastric radioactivity encountered by the scanner. The equation for power exponential fit (6),

$$f(T) = 2^{(-T/T50)(\beta)}$$

was applied in both the intragastric method and the abdominal method, in which $f(T)$ is the percentage of radioactivity remaining in the stomach at time T , compared with 100% at time 0. The curve-fitting parameters include estimates of T50 and β , which determines the shape of the curve ($\beta > 1$ indicates slow emptying progressing to rapid emptying; $\beta < 1$ indicates rapid emptying progressing to slow emptying). R^2 , representing the goodness of fit

in nonlinear curve fitting, was defined as $1 - \text{RSS}/\text{TSS}$, in which RSS is the residual sum of squares, and TSS is the total sum of squares (6). T50 was deemed noncalculable when the curve fitting failed or its value exceeded 300 min by computer calculation. The intragastric retention ratios at 30 (RR30), 60 (RR60), 90 (RR90), 120 (RR120) and 240 min (RR240) and T50 were obtained both by observation and by mathematical calculation. The observation values were obtained from original data for intragastric retention and interpolation for T50, not including data derived using the power exponential fit. The calculation data were derived from the power exponential fitting curve using two parameters (i.e., T50 and β), which were based on the initial 90 min of data. The differences between observed values and calculated values were used to evaluate the accuracy of fitting by each method.

To evaluate the efficiency of curve fitting in different emptying groups, the subjects were divided into normal and delayed emptying groups, using a threshold of 68% meal retention as measured with the intragastric method at 90 min (16). Data are expressed as mean \pm SEM and were analyzed using the Student paired t test. P values < 0.05 were considered statistically significant.

RESULTS

The intragastric method was applied to 23 subjects who had delayed gastric emptying (11 with diabetes and 12 with nonulcer dyspepsia) and 22 subjects with normal gastric emptying (10 healthy volunteers, 3 patients with diabetes and 9 with nonulcer dyspepsia). Table 1 shows the success of the rate of T50 calculation for the two methods. In the normal emptying group, T50 was always calculable using both the intragastric method and the abdominal method. In the delayed emptying group, however, the intragastric method was noncalculable for 16 of 23 subjects, and the abdominal method was noncalculable for only 3 subjects.

Table 2 shows that there was no significant difference between the calculated values of T50 for the abdominal and intragastric methods (120 ± 5 min versus 130 ± 6 min, $P = 0.25$). However, the intragastric method resulted in higher RR30 and RR60 than did the abdominal method ($P < 0.001$ and $P < 0.001$, respectively) and higher RR90, RR120 and RR240 without statistical significance. In the normal emptying group, all retention ratios, except RR30, between the two methods had no significant difference. However, in the delayed emptying group, RR30, RR60 and RR90 were

TABLE 1
Number of Subjects with Calculable T50 by Two Methods in Both Delayed and Normal Emptying Groups

Gastric emptying	Intragastric method		Abdominal method	
	Calculable T50	Noncalculable T50	Calculable T50	Noncalculable T50
Normal	22	0	22	0
Delayed	7	16	20	3
Total	29	16	42	3

T50 = half emptying time.

TABLE 2
Comparison of Parameters of Gastric Emptying Curve Using Intra-gastric Method and Abdominal Method

Parameters of gastric emptying	Normal emptying group		Delayed emptying group		Total	
	Intra-gastric method	Abdominal method	Intra-gastric method	Abdominal method	Intra-gastric method	Abdominal method
RR30	100 ± 3*	91 ± 2	113 ± 2*	97 ± 1	107 ± 2*	94 ± 1
RR60	80 ± 4	77 ± 2	104 ± 3*	90 ± 2	94 ± 3*	84 ± 2
RR90	62 ± 4	61 ± 3	94 ± 2*	86 ± 2	77 ± 3	73 ± 3
RR120	38 ± 4	39 ± 3	78 ± 4	74 ± 4	62 ± 6	58 ± 5
RR240	7 ± 1.5	8 ± 2.5	20 ± 4	18 ± 3	16 ± 5	14 ± 4
T50	115 ± 5	124 ± 6	141 ± 14	152 ± 10	120 ± 5	130 ± 6
R ²	0.87 ± 0.03*	0.97 ± 0.08	0.34 ± 0.07*	0.88 ± 0.04	0.75 ± 0.04*	0.94 ± 0.02

**P* < 0.05 significant difference between two methods by Student paired *t* test.

RR30 = retention ratio at 30 min; RR60 = retention ratio at 60 min; RR90 = retention ratio at 90 min; RR120 = retention ratio at 120 min; RR240 = retention ratio at 240 min; T50 = half emptying time; R² = goodness of fit in nonlinear curve fitting.

significantly higher for the intra-gastric method (*P* = 0.001, 0.001 and 0.05, respectively).

The abdominal method resulted in a significantly higher R² in both the normal and delayed emptying groups than did the intra-gastric method (0.97 ± 0.08 versus 0.87 ± 0.03, *P* = 0.001, and 0.88 ± 0.04 versus 0.34 ± 0.01, *P* = 0.005, respectively) (Table 2). In the normal emptying group, all of the R² values were able to be calculated by either the intra-gastric method or the abdominal method. However, for 10 subjects in the delayed emptying group, R² values not quantifiable using the intra-gastric method were successfully quantified using the abdominal method.

Lag phases were significantly longer in the delayed emptying group than in the normal emptying group (27.3 ± 5.2 min versus 19.3 ± 4.1 min, *P* < 0.05). However, when the intra-gastric method was used, the lag phases of the 16 subjects with noncalculable T50 were significantly longer than those of the 29 subjects with calculable T50 (28.1 ± 7.5 min versus 20 ± 5.9 min, *P* < 0.05).

Table 3 reveals that the differences between the observed values and calculated values of RR30, RR90, RR120 and T50 for the abdominal method were significantly smaller than for the intra-gastric method (3% ± 0% versus 22% ± 4%, *P* = 0.001; 6% ± 1% versus 10% ± 1%, *P* = 0.001; 14% ± 4% versus 27% ± 6%, *P* = 0.03; and 13% ± 4% versus 23% ± 5%, *P* = 0.02, respectively). However, there was no significant difference between the two methods in evaluating the differences between observed values and calculated values of RR60 and RR240 (5% ± 1% versus 4% ± 1%, *P* = 0.52, and 162% ± 43% versus 124% ± 17%, *P* = 0.12, respectively).

DISCUSSION

These data indicate that the new method of using the proportion of whole abdominal radioactivity to correct stomach radioactivity has three substantial advantages over the conventional intra-gastric method. First, the abdominal method resulted in more calculable T50s among subjects

with delayed gastric emptying than did the intra-gastric method; second, the goodness of fit of power exponential fit is generally better with the abdominal method than with the intra-gastric method, especially in patients with gastroparesis; and third, the differences between the observed values and calculated values of T50 and most retention ratios were smaller for the abdominal method than for the intra-gastric method.

Elashoff et al. (6) first proposed the power exponential for mathematical expression of biphasic characterization of gastric emptying. Liquid emptying is monoexponential and can adequately be described by a simple T50 value (19). Studies have shown that measurement of the rate of liquid emptying from the stomach requires less attenuation correction (9,14,20). Numerous scintigraphic studies have confirmed the biphasic nature of solid food gastric emptying

TABLE 3
Comparison of Difference for T50 and Retention Ratios Between Observation and Calculation Values Using the Two Methods

Parameters of gastric emptying	*Difference % (SEM)		Student paired <i>t</i> test (<i>P</i>)
	Intra-gastric method	Abdominal method	
RR30	22 (4)	3 (0)	0.001
RR60	4 (1)	5 (1)	NS
RR90	10 (1)	6 (1)	0.001
RR120	27 (6)	14 (4)	0.03
RR240	124 (17)	162 (43)	NS
T50	23 (5)	13 (4)	0.02

*Difference = percentage of difference between observation values and calculation values, or (calculation - observation)/observation × 100%.

RR30 = retention ratio at 30 min; RR60 = retention ratio at 60 min; NS = no statistical significance; RR90 = retention ratio at 90 min; RR120 = retention ratio at 120 min; RR240 = retention ratio at 240 min; T50 = half emptying time.

(12,13,21-23). Studies of solid food gastric emptying, in contrast to liquid emptying, have demonstrated the need for attenuation correction, particularly for characterizing the lag phase (11-14) and when, in some individuals, calculation of T50 is not feasible. Several methods have been used to minimize this defect, including geometric mean by antero-posterior scanning (11), posterior scanning with lateral correction (12), peak-to-scatter ratio (14) and LAO view (2,8,24). However, the fit of the empirical curve to the data by power exponential fit is poor during the early periods when the curve peaks; before gastric emptying, the curve diminishes even further during a postpeak delay (6).

Conventional methods of plotting the emptying curve by quantifying the amount of radioactivity within a gastric region of interest have neglected the contribution of postgastric radioactivity. Therefore, failure to calculate T50 by extrapolation is not unusual because of poor curve fitting or delayed gastric emptying. In this study, we took the radioactivity of the whole abdomen into account in plotting the emptying curve and gained substantial advantages for both curve smoothing and fitting, which were verified by general improvement of the goodness of fit and the fact that more calculable T50 values could be obtained by extrapolation. Moreover, we extended the observation time to 240 min to evaluate the accuracy of calculation by power exponential extrapolation based on 90 min of data. Again, the abdominal method generally has a smaller percentage of difference between observed values and calculated values than does the intragastric method, suggesting that the abdominal method has a substantial advantage in prediction of T50 by extrapolation.

There are three possible explanations for this phenomenon. First, gamma-ray attenuation resulting mainly from intragastric redistribution (anterior movement from fundus to antrum in the early phases after ingestion of a meal) may lead to significant underestimation of the rate of emptying using an anterior detector (11). Geometric mean by anterior-posterior scanning is supposed to be the gold standard for minimizing tissue attenuation. However, it is impractical in many centers to use two detectors, and an LAO view was thought to be an acceptable single-detector alternative (2,8,11,24). In this study, we used an LAO view, which was hypothesized to be positioned parallel to the stomach.

However, this is not the case in some individuals with anatomic variation, in whom technical difficulty may be encountered in confirming the parallel model. Therefore, in this study it was not unusual to encounter intragastric method retention ratios >100% in the early periods, especially among patients with gastroparesis associated with a prolonged lag phase. This early rise in the peak will not only lead to underestimation of the emptying rate, which is similar to the disadvantage of anterior view, but will jeopardize curve fitting and inevitably render the calculation of T50 by extrapolation inaccurate or impossible in some individuals. In contrast, when the abdominal method was used to plot the curve, the early rise in the peak in lag phase disappeared, and the fit of the curve dramatically improved because of its inherent characteristic and concomitant consideration of postgastric radioactivity.

Second, fluctuation in the curve may be caused by the movement of the subjects, which seems to be inevitable during a long period of recording (Fig. 1). Both the angle and the distance between the subject and the collimator are hard to keep constant throughout the whole procedure. Although two radioisotopic markers can minimize the problem, the validity of the end results still depends on the operator's skill. In our experience with the intragastric method, fluctuation of the curve may result in retention ratios even larger than 200% at a given time in one individual, rendering curve fitting impossible. The data in this study show that the abdominal method could ameliorate this problem. The explanation is that it is possible to minimize the variation of the intragastric count caused by fluctuations in the stomach-to-collimator distance by expressing the intragastric count as a proportion of the total abdominal counts, because both intragastric counts and intra-abdominal counts will change in the same direction when the distance between the subject and the collimator changes.

Third, duodenogastric retrograde flow, which is a normal physiological phenomenon, may also contribute to fluctuations in the emptying curve. However, there is currently no valid method for quantifying the reflux in scintigraphic gastric emptying studies. The possibility of retrograde flow induced by the curve fluctuation is low, because there is no evidence in this study of any prominent fluctuations in the

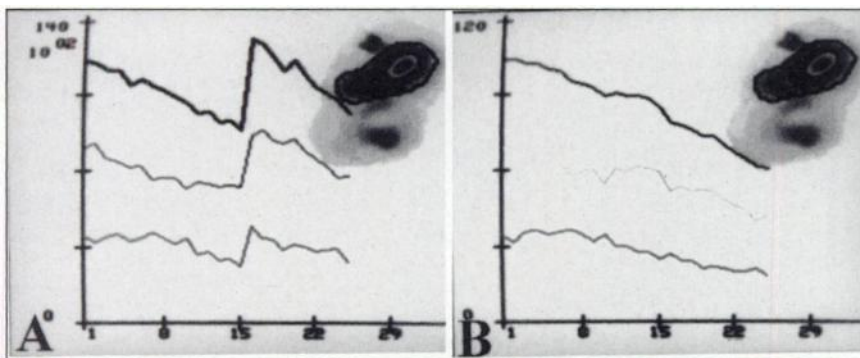


FIGURE 1. Example of radioactivity-time emptying curves in same study plotted by intragastric and abdominal methods. (A) Using intragastric method, upward fluctuation of curve happened during visit to toilet. (B) Abdominal method made them smooth. Upper, middle and lower curves are emptying curves of total, proximal and distal stomach, respectively.

curve that can be attributed simultaneously to decreasing small intestine radioactivity and increasing intragastric radioactivity.

Regarding the goodness of fit, R^2 significantly improved in almost all subjects when the abdominal method was used, and this enabled quantitative calculation of T50 in most subjects in whom it had been noncalculable using the intragastric method. It seems that R^2 should indicate whether a curve provides a good fit to the data, and therefore, a high R^2 (>0.9) should be a sign of a good fit. However, this is not the case in situations with a poor fit in a particular part of the curve, even when the R^2 value is high. Though R^2 usually exceeded 0.9 using the abdominal method, R^2 was not as high in the delayed emptying group as in the normal emptying group. One explanation of the inferior curve fits in the delayed emptying group, which usually had prolonged lag phases, is that the abdominal method resulted in observed points in a horizontal line during the lag phase and the intragastric method resulted in early rise in the peak or a postpeak delay, both of which jeopardized the curve fitting when the power exponential fit was applied (6).

CONCLUSION

Scintigraphic solid emptying curve fitting, based on the measurement of intragastric radioactivity as a proportion of the whole abdomen, is an alternative method for plotting the emptying curve and offers substantial advantages over the conventional intragastric method, especially in patients with gastroparesis. Whether this is valid in patients who have undergone postgastric surgery needs further evaluation.

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