Evaluation of an Inexpensive Screening Scintigraphic Test of Gastric Emptying

George M. Thomforde, Michael Camilleri, Sidney F. Phillips and Lee A. Forstrom

Gastroenterology Research Unit and Section of Nuclear Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

Our goal was to study the accuracy of a limited assessment relative to the traditional and obtain a more detailed approach to measure gastric emptying. **Methods:** We prospectively evaluated 35 patients referred to our laboratory with suspected fast or slow gastric emptying. Transit was measured radioscintigraphically after ingestion of an egg meal containing ^{99m}Tc-Amberlite pellets. Gastric emptying was analyzed by power exponential analysis. Diagnostic accuracy of simpler indices (gastric residual at 2 and 4 hr) was determined by comparing the categorization of patients as normal or abnormal relative to previously published normal data from our laboratory. **Results:** Gastric residual at 2 hr showed greater diagnostic accuracy for accelerated gastric emptying with 90% sensitivity at 90% specificity. Gastric residual at 4 hr was less accurate for accelerated emptying, but was more accurate at detecting delayed gastric emptying with 100% sensitivity at 70% specificity. In contrast, sensitivity and specificity of gastric residual at 2 hr for slow emptying were low (100% sensitivity with 20% specificity) emphasizing the importance of obtaining a scan later than 2 hr for detecting delayed gastric emptying. **Conclusion:** Selective scans taken at 2 and 4 hr provide an excellent screening test for detecting fast or slow gastric emptying; the accuracy of 2-hr data is optimal for accelerated emptying and that of the 4-hr data greater for delayed emptying. This strategy provides a simple, less expensive way to evaluate gastric emptying in clinical practice with acceptable sensitivity and specificity as an initial test for patients with clinically suspected gastric stasis or dumping syndromes.

Key Word: gastric emptying

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The scintigraphic gastric emptying test constitutes an important addition to the evaluation of patients with suspected motility disorders (*1*). However, the need for repetitive scanning usually required to assess the emptying rate constants from the stomach, as well as the time for the transfer of a defined proportion of isotope through the small intestine (*1,2*) results in considerable use of gamma camera and computer time and thus the relatively costly nature of these studies. Most of the currently used isotopic markers such as ^{99m}Tc-sulphur colloid added to egg or pancake may dissociate (*3*) from the digestible solid phase of the meal during emptying from the stomach and may reflect the emptying of the liquid phase. In contrast to in vivo radiolabeling of chicken liver, which has excellent binding characteristics for the isotope but is time consuming and does not lend itself to a high-volume practice, the radiolabeling of ion exchange pellets is a process that can be accomplished very rapidly (<5 min) (*2*).

Previous recovery studies have demonstrated that the isotope remains bound to the solid phase during its passage through the gastrointestinal tract (*2*). Having decreased the costs of preparation of the radiolabeling of the meal substrate, we have turned our attention to identify strategies that reduce the cost of the gastric emptying test by restricting the number of scans taken and, thus, the amount of gamma camera and computer time necessary to analyze the data. In a previous retrospective analysis (*4*), we have demonstrated that scans taken 2, 4 and 6 hr after the ingestion of a radiolabeled meal provide an appropriate representation of gastric emptying and small-bowel transit when compared to the more traditional, laborious and costly approach of repetitive measurements during a 4 to 6 hr period. The previous study was retrospective and included patients only with disorders associated with slow transit in the stomach and small bowel, such as diabetic neuropathy and progressive systemic sclerosis. In the current study, our aim was to prospectively evaluate the use of the same scanning procedure at 2 and 4 hr following the ingestion of a radiolabeled solid meal in order to evaluate the diagnostic accuracy of this procedure relative to the more laborious, detailed measurements that require repeated, regular scans, usually taken at 15- to 30-min intervals.

MATERIALS AND METHODS

Patients and Volunteers

We evaluated 35 patients referred to our laboratory for suspected abnormalities of gastric and/or small-bowel motility. We defined gastric emptying by power exponential analysis (κ = the emptying rate constant). We then assessed the diagnostic accuracy of a simpler analysis, i.e., the gastric residual at 2 and 4 hr. Patient data were characterized as normal, fast or slow transit by comparison with normal values (n = 37) previously published; i.e., gastric emptying κ of 41 to 66 $\times$ 10^{-4} (*4*).

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For correspondence or reprints contact: Dr. Michael Camilleri, Gastroenterology Research Unit, Mayo Clinic, Rochester, MN 55905.

TABLE 1
Stability of Binding of ^{99m}Tc to Amberlite 410A Pellets

	Mean percentage radioactivity in supernatant (unbound to solid phase)		
	Hr 1	Hr 2	Hr 3
Amberlite 410-^{99m}Tc-pertechnetate in egg	0.8	1.2	1.2
^{99m}Tc-sulfur colloid in egg	4.6	7.5	9.6

In Vitro Binding of Radiolabel to Ion Exchange Pellets

We used a previously published (*3*) in vitro stomach model to evaluate stability of binding of isotope to its substrate. Briefly, this consisted of a beaker containing 500 ml of N saline, into which we continually infused 0.2 N hydrochloric acid (containing 1200 units pepsin/ml) at a rate of 20 ml/hr; the contents were stirred at 120 RPM, and the pH at the start of the experiment was 6.5, and at the end of 3 hr was 1. A 10-ml aliquot was taken every hour for 3 hr to determine proportion of radioactivity in the supernatant after centrifugation. We tested Amberlite IRA-410 ion exchange pellets (Sigma Chemical Co., St. Louis, MO) labeled with 0.5 mCi of ^{99m}Tc-pertechnetate which were mixed with an egg and cooked. The latter was cut into small pieces before being added to the saline. Experiments were performed in triplicate, and ^{99m}Tc-sulfur colloid cooked in egg was used as control.

In Vivo Experimental Procedure

After an overnight fast, patients were fed a radiolabeled breakfast consisting of two eggs, one slice of whole wheat bread and 240 ml of skim milk. The caloric value of the meal was 284 kcal, with a nutrient composition of 31% protein, 32% carbohydrate, 37% fat and 2.5 g of fiber. The isotope used in labeling the meal was 1.0 mCi of pertechnetate which was incorporated on to Amberlite IRA-410 anion exchange resins. The polystyrene pellets were mixed into the raw eggs and then cooked to a firm consistency before being served. Table 1 shows the stability of binding in an acid-peptic milieu of ^{99m}Tc to Amberlite 410A pellets using an in vitro technique that has been previously published (*3*).

Gamma Camera Imaging

Imaging was performed with a large field-of-view gamma camera with a medium energy, parallel hole collimator (GE Starcam, Milwaukee, WI). Anterior and posterior images were acquired with the subjects erect. Static 2-min images were acquired for each time period. A window set at 140 keV ±10% was used to collect the data. Scans were obtained every 15 min during the first hour at half-hour intervals during the next 3 hr in 17 patients and at 0, 2 and 4 hr in the remaining 18 patients. All patients received a 500 kcal meal within 15 min prior to the 4-hr scan.

Data and Statistical Analysis

Gastric Emptying. Regions of interest were drawn around the stomach of the anterior and posterior image for each time frame. To correct for attenuation, the counts of each were multiplied together and the square root of the product was taken to obtain the geometric mean. Gastric emptying was expressed according to simplified and detailed analyses. The percentage of isotope in the stomach was also quantitated at 2 and 4 hr, and compared to that of normal ranges (2 hr GE, 53%–76% and 4 hr GE, 0%–40%) (*4*). In 17 patients, scans were taken at 15-min intervals during the first

TABLE 2
Accuracy (%) of Simplified Versus Detailed Analysis in 17 Patients

Detailed analysis	1.88 ± 0.24	0.0046 ± 0.0006
Scans at 0, 2 and 4 hr	2.38 ± 0.41	0.0052 ± 0.0009
p value (paired t-test)	>0.1	>0.5

4 hr, so that gastric emptying could be analyzed by means of a power exponential model: $prop_t = \{-(\kappa^* t)^{\beta}\}$, where $prop_t$ is the proportion remaining at time t (*1*). The index κ is an expression of the instantaneous slope of the curve and β is the shape of the curve ($\beta \leq 1$ implies a simple exponential emptying curve) (*5,6*). The parameters κ and β were estimated using the NLIN procedure in the SAS software package (SAS Institute, Cary, NC).

In a preliminary analysis of the first 17 patients, we had shown that estimates of κ and β were not statistically different when using all the data points versus using only data at 0, 2 and 4 hr (Table 2). In the next 18 patients, we acquired data only at 0, 2 and 4 hr.

For the gastric residual at 2 and 4 hr, we estimated the spectrum of sensitivities and specificities in patients with accelerated or delayed transit using a receiver operating characteristic curve (ROC) (*7,8*).

RESULTS

Assessment of Gastric Emptying

Using the previously published norms, gastric emptying was normal in 10, slow in 15 and fast in 10 patients. Figure 1 shows an example of a patient with accelerated gastric emptying. Note that κ, from power exponential analysis of the gastric emptying curve, was rapid at 76×10^{-4}. Note that the triangles, which summarize the data at 2 hr after ingestion of the meal, show values that are outside the normal range at 2 hr. A similar example of gastric emptying in a patient with slow transit is demonstrated in Figure 2 where the gastric emptying κ is 35×10^{-4}. Again, notice the triangle designates delay in transit through the stomach at 2 and 4 hr.

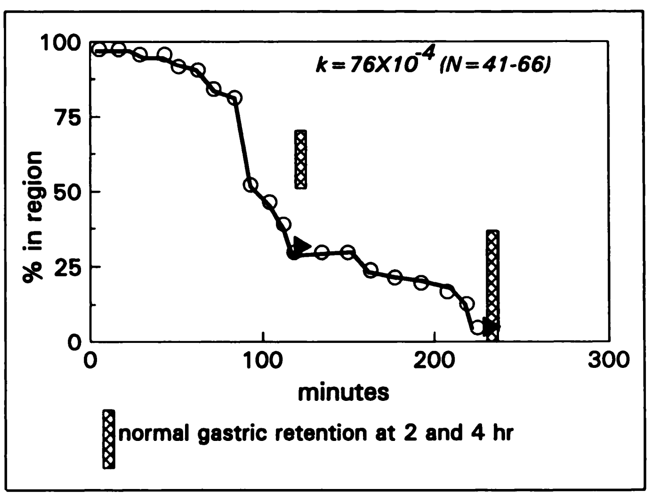

FIGURE 1. Example of gastric emptying curve in a patient with rapid transit (k as shown). Note that the simplified analysis at 2 hr correctly detects rapid transit relative to normal data.

Comparison of Simple Indices with Detailed Analysis

The residual content of the stomach at 2 and 4 hr indicated only one false-positive and five false-negatives, two in the slow emptying and three in the fast emptying groups. Gastric residual at 2 hr was relatively more sensitive and specific in identifying fast gastric emptying (Fig. 3). Three of 10 patients with high κ values from power exponential analysis showed normal emptying at 2 hr and all had a completely empty stomach at 4 hr, suggesting later acceleration of emptying. Gastric residual at 2 hr was relatively less sensitive and specific in patients with slow gastric emptying. In Figure 3, at 100% sensitivity, specificity for fast transit was 70%, and for slow transit, only 20%. The ROC curve for gastric retention at 2 hr departs insignificantly from the ideal estimate of fast gastric emptying, that is, κ. In this sample of patients, the 4-hr scan added significantly to the accuracy of the gastric data at 2 hr in assessing patients with slow gastric emptying. Thus, 4 of 15 patients with slow gastric emptying κ had abnormal gastric residual at 4 hr, but normal residual at 2 hr. While the sensitivity for gastric residual at 4 hr was excellent, the specificity was less than optimal (see Fig. 3, 60% specificity at 100% sensitivity).

DISCUSSION

Our data shows the use of a simple approach to measuring gastric emptying that involves the use of a gamma camera for a short period of time in contrast to the traditional method. Selective scans were taken 2 and 4 hr after ingestion of a radiolabeled solid meal and provide an excellent screening test for the detection of both accelerated and delayed gastric emptying. The 2-hr data were more accurate for accelerated than for delayed gastric emptying. The gastric residual at 4 hr was more accurate than the gastric residual at 2 hr in detecting delayed emptying, was less specific as an indicator of accelerated gastric emptying, and, if used as the only measurement would clearly miss the initial rapid transit through the stomach.

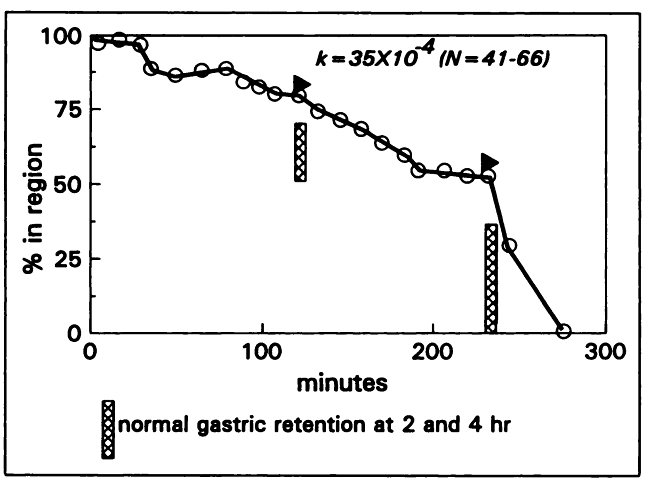

FIGURE 2. Example of gastric emptying curve in a patient with slow transit (k as shown). Note that the simplified analyses (solid triangle) at 2 and 4 hr correctly detect slow gastric emptying relative to normal data.

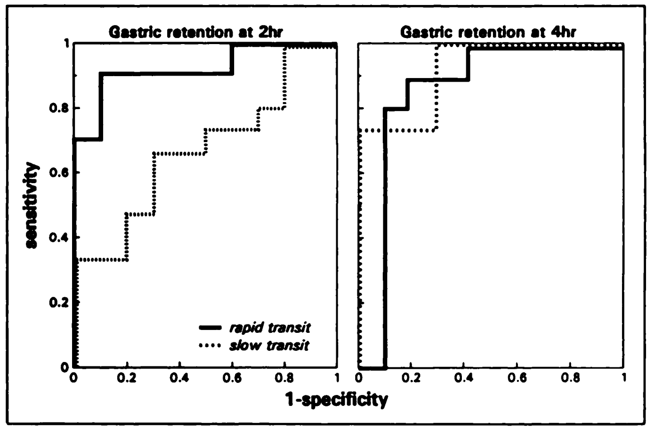

FIGURE 3. ROC curves of gastric residual at 2 hr and 4 hr compared to k from power exponential analysis of the gastric emptying curves of 35 patients (15 slow, 10 fast and 10 normal gastric emptying).

Our study has important implications for the containment of costs in the measurement of gastric emptying in clinical practice by: using radiolabeled ion exchange pellets (which require a minimum time for isotopic labeling and preparation), and by restricting the number of scans taken during these studies and the time taken for computer analysis of the data. We have been able to reduce the cost of the gastric emptying test by a factor of four. This strategy does not permit the measurement of the gastric lag time, during which solids are retained in the stomach. The lag time is an indicator of distal antral pressure activity in response to a meal in health and disease (*9*), however, the proportion of the meal emptied (or fractional emptying rate) is an alternative measure which has probably greater practical significance to the clinician (*1,2,9*).

As a result of this strategy, our practice in assessing patients with suspected motility disorders has changed (*10*). Thus, the gastric emptying test is used more appropriately as an initial, or screening, method to evaluate patients with apparently functional gastrointestinal symptoms who may have significant motility disorders causing stasis or dumping. Functional disorders constitute the vast majority of patients with gastrointestinal symptoms who present to outpatient gastroenterology clinics in the western world (*11,12*). The availability of an inexpensive but accurate screening test provides a method to identify those with bonafide motility disorders that require further investigation or treatment (*10,13*). It is also possible that in the future, the dose of ^{99m}Tc could be reduced further, while increasing the imaging time without significantly increasing the use of a gamma camera or costs of these studies.

Interpretation of a single transit measurement should always be viewed with caution since there is undoubtedly day-to-day variability in the transit through the stomach and small intestine. Preliminary data, however, on the reproducibility of such measures from our unit (Degen L, Phillips SF, *personal communication*) confirm those of Collins et al. (*14*) who demonstrated that gastric emptying parameters such as the fractional emptying rates from the stomach are relatively constant in the human gastrointestinal tract.

The approach previously proposed (*4*) to develop a relatively inexpensive test for gastric emptying disturbances has proven to be accurate in a prospective evaluation of the technique; this continues to be an important area where the nuclear medicine laboratory can contribute significantly to the rapid, noninvasive and cost-effective evaluation of patients with common gastrointestinal symptoms such as nausea, vomiting and bloating.

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REFERENCES

1. Camilleri M, Malagelada J-R, Brown ML, Becker G, Zinsmeister AR. Relation between antral motility and gastric emptying of solids and liquids in humans. *Am J Physiol* 1985;249:G580–G585.
2. Camilleri M, Colemont LJ, Phillips SF. Human gastric emptying and colonic filling of solids characterized by a new method. *Am J Physiol* 1989; 257:G284–G290.
3. Thomforde GM, Brown ML, Malagelada J-R. Practical solid and liquid phase markers for studying gastric emptying in man. *J Nucl Med Technol* 1985;13:11–14.
4. Camilleri M, Zinsmeister AR, Greydanus MP, Brown ML, Proano M. Towards a less costly but accurate test of gastric emptying and small bowel transit. *Dig Dis Sci* 1991;36:609–615.
5. SAS Users Guide: Statistics. Cary, North Carolina, SAS Institute, 1982, pp. 15–37, 297–308.
6. *SUGI supplemental library user's guide*. Cary, NC. SAS Institute; 1986: 269–293.
7. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982;143:29–36.
8. Metz CE. Basic principles of ROC analysis. *Semin Nucl Med* 1978;8:283–298.
9. Camilleri M, Brown ML, Malagelada J-R. Relationship between impaired gastric emptying and abnormal gastrointestinal motility. *Gastroenterology* 1986;91:94–99.
10. Camilleri M. Study of human gastroduodenojejunal motility: applied physiology in clinical practice. *Dig Dis Sci* 1993;38:785–794.
11. Switz DM. What the gastroenterologist does all day. *Gastroenterology* 1976;70:1048–1050.
12. Lennard-Jones JE. Functional gastrointestinal disorders. *N Engl J Med* 1983;308:431–435.
13. Camilleri M, Prather CM. The irritable bowel syndrome: mechanisms and a practical approach to management. *Ann Intern Med* 1992;116:1001–1008.
14. Collins PJ, Horowitz M, Cook DJ, Harding PE, Shearman DJ. Gastric emptying in normal subjects: a reproducible technique using a single scintillation camera and computer system. *Gut* 1983;24:1117–1125.