The Utility of Adding a Liquid-Nutrient Meal to Aid Interpretation of Small-Bowel Transit Scintigraphy

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J Nucl Med Technol 2021; 49:132–137
DOI: 10.2967/jnmt.120.255091

Small-bowel transit scintigraphy (SBTS) evaluates the accumulation of a radiolabeled meal in the terminal ileal reservoir (TIR) 6 h after ingestion. The location of the TIR may be difficult to determine because anatomic information is limited; for equivocal studies, the patient is asked to return the next day to help determine the TIR location by potential transit into the colon. The purpose of this study was to evaluate whether administration of an additional liquid-nutrient meal (LNM) at 6 h can promote movement of the radiolabeled meal to aid in the interpretation of SBTS and eliminate the need for the patient to return. **Methods:** This retrospective study reviewed 117 SBTS studies from February 2017 to September 2019. Patients were fed a standardized mixed radiolabeled solid–liquid meal for gastric emptying with SBTS according to Society of Nuclear Medicine and Molecular Imaging practice guidelines. An additional LNM was given at 6 h, and post-LNM images were obtained at least 20 min after the LNM. Two board-certified nuclear medicine physicians independently evaluated all images as equivocal or diagnostic at 6 h. **Results:** Of the 117 patients (71.8% female; median age, 42.0 y) undergoing SBTS, 37 were equivocal cases at 6 h before the LNM (31.6%; 95% CI, 23.3%–40.9%), compared with 12 equivocal cases after the LNM (10.3%; 95% CI, 5.4%–17.2%). Of the equivocal cases, 25 (69.4%; 95% CI, 51.9%–83.7%) had a definitive result after the LNM, whereas 11 (30.6%; 95% CI, 16.4%–48.1%) remained equivocal and 1 showed rapid transit. Among the 23 patients with gastroparesis, only 13 (57%) responded to the LNM, and none of the 3 patients with irritable bowel syndrome responded. **Conclusion:** The number of equivocal SBTS cases decreased after administration of an LNM at 6 h, converting to a definitive result. This suggests that with use of an LNM, most patients can complete SBTS in 1 d without the need for repeat imaging at 24 h. Administering an LNM appears to be less effective for patients with gastric disorders. However, the clinical significance remains to be explored, and it is unclear whether such patients have both a gastric and a small-bowel disorder, hence reducing any motility-promoting effect of the LNM.

Key words: small-bowel transit scintigraphy; liquid-nutrient meal; gastrointestinal dysmotility; gastroparesis; irritable bowel syndrome

Received Aug. 09, 2020; revision accepted Dec. 04, 2020.
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Published online Dec. 24, 2021.

Small-bowel dysmotility can be seen in an array of gastrointestinal tract disorders, such as irritable bowel syndrome, chronic idiopathic intestinal pseudoobstruction, chronic constipation, chronic diarrhea, small-intestinal bacterial overgrowth, and celiac disease (*1–3*). Individuals with underlying neuropathies or myopathies may also manifest symptoms of small-bowel dysmotility (*1*,*4*). These symptoms include abdominal pain, diarrhea, constipation, abdominal distension, bloating, nausea, or vomiting (*2*,*3*,*5*). Given these nonspecific symptoms, differentiating between upper- and lower-gastrointestinal-tract dysfunction in patients with suspected motility disorders can be challenging. Evaluating small-bowel motility may provide diagnostic information (*6*).

Gastric emptying scintigraphy is recognized as the gold standard for analyzing gastric motility, as it uses a physiologic meal to provide accurate quantification of the emptying of a meal from the stomach over the course of 4 h (*2*). Small-bowel transit scintigraphy (SBTS) is increasingly being used as a continuation of the standard gastric emptying scintigraphy. SBTS allows for the determination of either orocecal leading-edge transit of a radiolabeled meal (the first visualized arrival of activity in the cecum) or measurements of the overall bulk transit of the meal into the terminal ileal reservoir (TIR) (*7*). Clinical indications for SBTS include known or suspected gastroparesis, irritable bowel syndrome symptoms, dyspepsia, scleroderma, and malabsorption, particularly if there are ongoing symptoms and prior normal results on gastric emptying scintigraphy. Current guidelines for SBTS require measurement of a standardized mixed solid–liquid radiolabeled meal 6 h after ingestion (*8*). SBTS is considered normal if more than 40% of the administered solid–liquid meal activity has progressed into the TIR or into the cecum or ascending colon at 6 h (*9*). Accurate identification of the TIR can be difficult because of the lack of anatomic information available in scintigraphic images and may render the study result equivocal at 6 h. Additionally, correlation with other anatomic imaging modalities such as abdominal radiography or CT is not always available. As such, patients with an equivocal study often need to return at 24 h to confirm the location of the colon, which typically will be visualized the next day. Returning the following day is often problematic and impractical for patients.

Meal ingestion facilitates the transfer of chyme from the TIR to the colon in bolus movements that correspond to ileal contractions (*10*). After ingestion of a meal, the number of boluses increases with simultaneous colonic filling, implying a gastroileal reflex (*10*). The purpose of this study was to investigate whether the administration of a highly caloric liquid-nutrient meal (LNM) at 6 h can stimulate progression of the radiolabeled meal to help identify loops of distal small bowel and the TIR location or potential transit into the colon. We additionally correlated patients' clinical symptoms and diagnoses to the response to administration of an LNM to determine whether certain conditions are more predictive of a positive or equivocal response.

MATERIALS AND METHODS

Study Design

Our institutional review board (Lewis Katz School of Medicine at Temple University) approved this retrospective study, and the requirement to obtain informed consent was waived. The patients included those sent for SBTS because of suspected small-bowel dysmotility at our institution between February 1, 2017, and September 1, 2019. All studies were anonymized as per institutional review board regulations and presented to the readers in random order with a delay of at least 6 mo from the time of the original clinical study to help prevent any unmasking.

Patients were fed a standardized mixed solid-plus-liquid meal as specified in the Society of Nuclear Medicine and Molecular Imaging guidelines (*8*). The solid-meal egg white was radiolabeled with approximately 18,500 kBq (500 μCi) of ^{99m}Tc-sulfur colloid. The liquid portion of the meal consisted of approximately 4,625 kBq (125 μCi) of ^{111}In-diethylenetriaminepentaacetic acid in 177 mL (6 oz) of water administered with the egg-white-meal sandwich. The unlabeled portion of the meal consisted of 2 pieces of white toast plus 30 g of jam and the labeled portion, egg white. Images of the abdomen were then obtained in both anterior and posterior projections for 6 h after meal ingestion to record small-bowel transit. From these images, liquid gastric emptying at 1 h and small-bowel transit at 6 h were measured.

The LNM that we used in this study is a commercially available 237-mL (8 oz) bottle of liquid containing 360 kcal, 14 g of protein, 45 g of carbohydrates, 3 g of fiber, 22 g of sugar, and 14 g of fat. All patients received the LNM at the 6-h time point during their SBTS regardless of the result of the SBTS, to reduce variations and differences in practice between clinicians. Those patients who underwent repeat imaging 20 min afterward were included in the study.

Patient demographic information at the time of the SBTS was obtained, including age, sex, race (our findings may not be generalizable to every patient population), symptoms, and final diagnosis from the electronic medical record. All images were independently reviewed by *2* board-certified nuclear medicine physicians. The interpretation of the SBTS images was recorded as normal transit, abnormally delayed transit, or equivocal transit based on 6-h images before and after the supplemental LNM. SBTS findings were considered normal if more than 40% of the administered liquid-meal activity had progressed into the TIR or passed into the cecum or ascending colon at 6 h (*9*).

Representative images are shown in Figures 1–4. Figure 1 demonstrates a normal SBTS result, in which there is an accumulation of activity within the TIR and into the colon. Figure 2 describes an abnormal result, in which there is no distal small-bowel accumulation, with diffuse activity throughout the small bowel.

An equivocal finding was defined as any uncertainty by the reader that the liquid-meal activity had progressed into the TIR. Figure 3 demonstrates an equivocal case that responded to the LNM. In this case, the pre-LNM images showed some progression of activity into the right lower quadrant, but it was unclear whether this activity represented filling of the TIR. After the LNM, there was clear progression of activity from the right lower collection into the cecum and ascending colon, confirming the location of the TIR before LNM administration. For the findings to be considered changed from equivocal to definitively normal or delayed small-bowel transit, the reader had to be certain that focal activity in the right lower quadrant progressed directly into the cecum or ascending colon or that questionable loops of nonfocal small-bowel activity all progressed farther into a single focal area consistent with the TIR.

The readers' interpretations of pre-LNM and post-LNM images were obtained simultaneously. Supplemental Table 1 shows a frequency count of all combinations of pre-LNM results recorded by the 2 readers (supplemental materials are available at http://jnm.snmjournals.org). Only cases that were mutually agreed on by the 2 readers at the pre-LNM time point were included in the main analysis, as shown in Supplemental Figure 1. This criterion prevented the introduction of bias through reviewing images repeatedly. Only disagreements on the post-LNM images between the 2 readers were adjudicated by a third independent board-certified nuclear medicine physician. Patients with rapid small-bowel transit

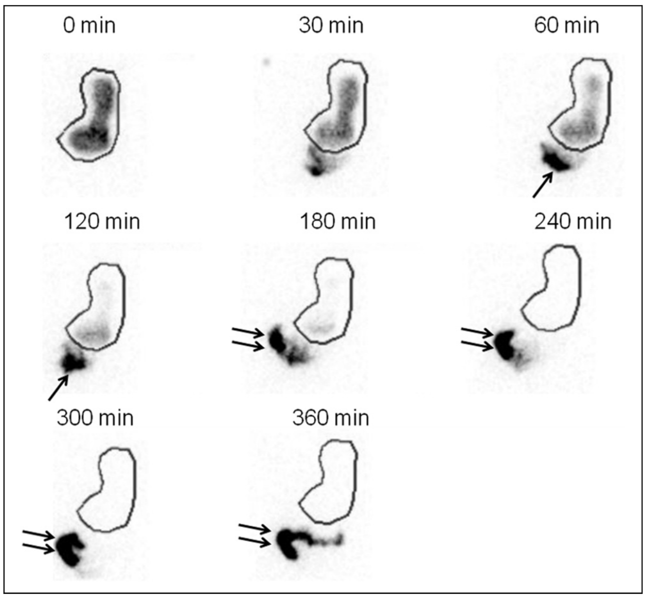

FIGURE 1. A 20-y-old man with nausea and vomiting who underwent sequential gastric emptying imaging, which showed normal small-bowel transit. There was normal progressive filling of TIR (single arrows) and then early progression into cecum and colon (double arrows) (anterior views). More than 40% of total activity had progressed from TIR into colon by 360 min.

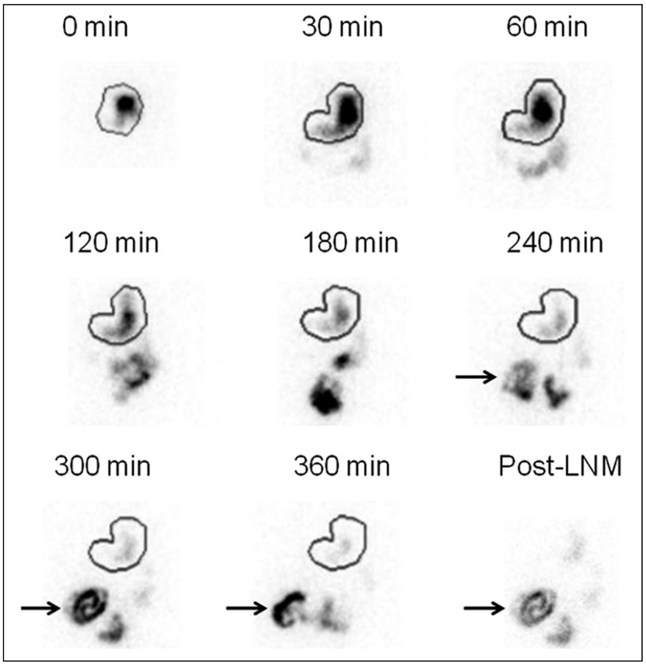

FIGURE 2. A 30-y-old man with nausea, vomiting, abdominal pain, and weight loss who underwent SBTS and was found to have delayed or abnormal small-bowel transit (anterior views). In contrast to patient in Figure 1, there was persistent and diffuse activity within loops of proximal small bowel and no accumulation of activity in TIR (arrows) by 360 min. There was no change in pattern of more proximal loops of small bowel after administration of LNM.

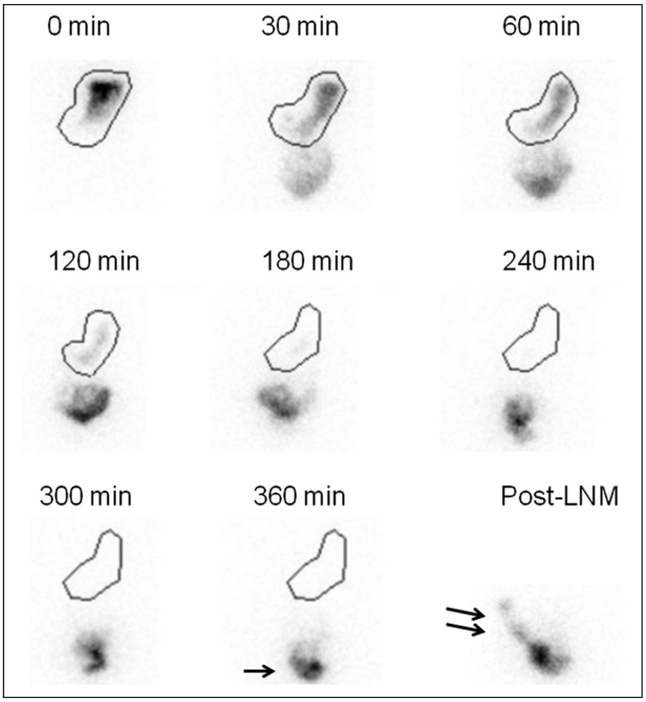

FIGURE 3. A 27-y-old woman with nausea, diarrhea, bloating, and abdominal distention who had equivocal SBTS findings but confirmation of TIR and colon localization after administration of LNM (anterior views). There was progression of activity into right lower quadrant, but it was unclear whether this finding represented filling of TIR by 360 min (single arrow). After LNM, however, anatomy was more clearly defined, showing normal progression of activity from TIR into colon (double arrows).

were excluded because these patients were not expected to respond to the stimulating effect of the LNM.

The readers were masked to all clinical data and interpreted the images more than 6 mo after the initial study was performed. This interval helped to ensure that the readers carried no prior clinical biases and removed the interpretation and selection process from the clinical practice. All 3 readers were masked to the primary and secondary outcomes until all data collection was complete.

The primary goal was to determine the proportion of patients for whom identification of the TIR and transition to the colon at 6 h had initially been inconclusive but became definitive after administration of the LNM. One secondary goal was to compare the clinical diagnoses of patients who responded to an LNM with the clinical diagnoses of patients who did not. Another secondary goal was to perform a subset analysis of factors that may predict a response to an LNM.

Statistical Analysis

For continuous variables, descriptive summary statistics are presented as means with SDs or as medians with ranges. For categoric variables, descriptive summary statistics are presented as frequencies with percentages. The Clopper–Pearson exact method was used to calculate binomial 95% CIs for proportions. The Fisher exact test was used to test for associations between 2 categoric variables, and the Wilcoxon rank test was used to determine associations between continuous covariates and a response outcome. Collected data were managed in Microsoft Excel. Statistical data analyses were performed using SAS, version 9.4 (SAS Institute Inc.).

RESULTS

Patient Characteristics

Between February 1, 2017, and September 1, 2019, SBTS was performed on 117 patients (71.8% [84/117] female; 83.8% [98/117] White; median age, 47 y; age range, 19–70 y) at our institution. Patient demographics are shown in Table 1. One case showed early rapid small-bowel transit and was removed from the cohort because the rapid transit obviated the LNM.

Effectiveness of an LNM on Equivocal Cases

Before the LNM, 37 of the 117 cases had concordant equivocal results and 80 had definitive diagnostic results of normal or delayed small-bowel transit (Table 2). The percentage of equivocal cases decreased from 31.6% (37/117) (95% CI, 23.3%–40.9%) before the LNM to 10.3% (12/117) (95% CI, 5.4%–17.2%) afterward. For 25 of the 37 equivocal cases, the LNM helped with interpretation of the study; 16 had normal small-bowel transit and 9 had delayed small-bowel transit. Of the 37 equivocal pre-LNM cases, 1 case was removed from the cohort after adjudication because it demonstrated rapid transit to the colon. Therefore, only 36 cases completed the subsequent analysis. Supplemental Table 2 describes the frequency of pre-LNM equivocal cases that yielded a post-LNM definitive result. Of the

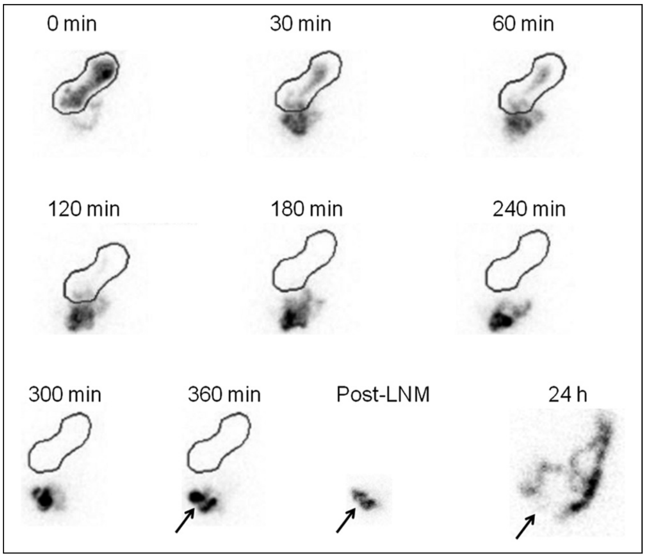

FIGURE 4. A 17-y-old boy with abdominal pain and early satiety who had equivocal SBTS findings at 6 h (anterior views). Although there was accumulation of activity in right lower quadrant at 6 h (arrow), this activity did not clearly progress into cecum or ascending colon after LNM. A 24-h image, however, helped to better define anatomy and showed that site of buildup in right lower quadrant (arrow) was in TIR, with progression of activity into ascending, transverse, and descending colon, confirming normal small-bowel transit.

36 equivocal cases, 25 (69.4% [25/36]; 95% CI, 51.9%–83.7%) had a definitive result after LNM (16 had normal results, and 9 had abnormal results), whereas 11 (30.6% [11/36]; 95% CI, 16.4%–48.1%) remained equivocal. Only 4 of these 11 cases had a 24-h study completed the following day.

Clinical Characteristics Correlating with an Effective LNM

To further understand the clinical utility of administering an LNM, clinical characteristics were compared between equivocal cases that showed a definitive result after the LNM and those that remained equivocal. Table 3 compares the basic demographics, symptoms, and subsequent diagnoses. Gastroparesis and irritable bowel syndrome (IBS) were significantly associated with a negative response to an LNM when comparing equivocal cases with definitive cases, at 90.9% (10/11) vs. 52.0% (13/25) ($P = 0.031$) and 27.3% (3/11) vs. 0.0% (0/25) ($P = 0.023$), respectively. Additionally, the symptom of early satiety appeared to be associated with a definitive response after LNM (9.1% [1/11] vs. 44.0% [11/25]); however, it did not reach statistical significance, with a P value of 0.059.

TABLE 1
Patient Demographics and Clinical Information

Baseline characteristic	Data
Median age (y)	42 (range, 17–81)
Sex	
Male	33 (28.2)
Female	84 (71.8)
Race	
White	98 (83.8)
Black	8 (6.8)
Hispanic	10 (8.5)
Mixed	1 (0.9)
Body mass index	
≤19	15 (12.8)
20–24	32 (27.4)
25–29	37 (31.6)
≥30	33 (28.2)
Symptoms	
Nausea	94 (80.3)
Vomiting	76 (65.0)
Abdominal pain	47 (40.2)
Early satiety	42 (35.9)
Weight loss	29 (24.8)
Bloating/distention	38 (32.5)
Diarrhea	30 (25.6)
Constipation	15 (12.8)
Decreased appetite/anorexia	9 (7.7)
Belching	6 (5.1)
Diagnosis	
Gastroparesis	63 (53.8)
Cyclic vomiting syndrome	8 (6.8)
IBS	10 (8.5)
SIBO	32 (27.4)
Malignancy	1 (0.9)
GERD	16 (13.7)
Dumping syndrome	1 (0.9)
Unspecified	17 (14.5)

SIBO = small intestinal bacterial overgrowth; GERD = gastroesophageal reflux disease.

Except for age, data are numbers followed by percentage in parentheses; $n = 117$ patients total.

DISCUSSION

The aim of this study was to examine whether the administration of an LNM helped facilitate visualization of the TIR and colonic transit in SBTS cases that were equivocal at the standard 6-h time point. Our results show that the number of equivocal SBTS cases significantly decreased after administration of an LNM at 6 h, with most cases converting to a definitive result. This finding has clinical relevance, as it allows a subset of patients to complete the study in one encounter without the inconvenience of returning for repeat imaging at 24 h. Difficulty in reliably identifying anatomic landmarks for the TIR and cecum, as well as the time-consuming nature of SBTS, are often cited as significant disadvantages to SBTS (*11*,*12*). However, the effect of an LNM on promoting movement of the radiolabeled liquid meal distally into the small bowel or into the colon allows for improved identification of these anatomic landmarks and decreases the need for repeat imaging at 24 h. Thus, when imaging findings are equivocal at 6 h, administration of an LNM should be considered routine.

In assessing the clinical characteristics correlating with an effective LNM, we noted that gastroparesis and IBS were predictive of a negative response to the LNM.

TABLE 2
SBTS Results Before and After Administration of LNM

Result	Before LNM	After LNM
Definitive	80 (68.4)	105 (89.7)
Normal	58 (49.6)	74 (63.2)
Abnormal	22 (18.8)	31 (26.5)
Equivocal	37 (31.6)	12 (10.3)

Data are numbers followed by percentage in parentheses; n = 117 patients total.

However, there are several distinct etiologies of gastroparesis, including diabetic, postsurgical, and idiopathic (*13*). The fact that the various etiologies of gastroparesis were grouped together may account for the observed negative responses. With regard to IBS, it is well documented that these patients may have small-bowel dysmotility and, thus, that a negative response to an LNM may be anticipated (*14*,*15*). However, alterations in sensory and motor gut function have been demonstrated to differ among IBS subgroups (i.e., diarrhea-predominant, constipation-predominant, or alternating) (*15*). The fact that all subgroups of IBS were grouped together in this study may account for the overall observed negative response to an LNM among IBS patients. From a clinical perspective, perhaps the patients with gastric disorders had both gastric and small-bowel dysfunction and the LNM could not stimulate any additional motility because these patients were symptomatic. Hence, the effect of using an LNM in patients with gastric disorders remains unclear and warrants further study.

There were several limitations to this study. The study standardization required at least a 20-min wait after administration of the LNM before capture of the first post-LNM image. On review of this interval to ensure no confounding effect, we found that some images had been obtained earlier than 20 min. If post-LNM images are obtained too soon, there may not be enough time for the LNM to exert a promotility effect. However, our results demonstrated that the number of equivocal SBTS cases converting to a definitive result remained significant regardless of the sometimes shortened waiting period.

Another study limitation was interobserver variability, which is not limited to SBTS but is well documented in scintigraphy and in radiology in general (*16*–*18*). A post hoc analysis revealed a concordance rate of 55% (65/117) between the 2 primary readers for the pre-LNM results—similar to what has been documented in the literature (*16*,*17*). We also recognize that our use of third-reader adjudication in cases of discordance between the 2 primary readers is not a perfect gold standard, but such adjudication is accepted in clinical trials by regulatory agencies such as the Food and Drug Administration (*19*).

Because only 4 patients underwent confirmatory 24-h studies, conclusions on the value of 24-h imaging cannot be drawn. A contributing factor limiting our use of 24-h imaging is that patients undergoing SBTS at our institution are typically scheduled for a hydrogen breath test the next day. Repeat imaging at 24 h is of limited utility if the patient undergoes a hydrogen breath test earlier in the day, as each test can interfere with the other (*20*,*21*). Despite there being no confirmatory study, our result still showed a nearly 70% rate of response to LNM, suggesting its applicability in clinical practice.

Our study analysis was directed primarily toward evaluation of delayed small-bowel transit (and cannot be extrapolated to patients with rapid transit). Rapid small-bowel

TABLE 3
Comparison of Baseline Characteristics Between Equivocal Cases That Showed Definitive Result After LNM and Those That Remained Equivocal

Characteristic	All (n = 36)	Definitive (n = 25)	Equivocal (n = 11)	P
Median age (y)	40 (range, 19–70)	40 (range, 19–70)	35 (range, 20–69)	0.52
Sex				
Male	6 (17)	5 (20)	1 (9.1)	0.64
Female	30 (83)	20 (80)	10 (91)	
Race				
White	29 (81)	21 (84)	8 (73)	0.096
Black	3 (8.3)	3 (12)	0 (0.0)	
Hispanic	3 (8.3)	1 (4.0)	2 (18)	
Mixed	1 (2.8)	0 (0.0)	1 (9.1)	
Body mass index				
≤19	6 (17)	5 (20)	1 (9.1)	0.70
20–24	11 (31)	6 (24)	5 (45.5)	
25–29	8 (22)	6 (24)	2 (18.2)	
≥30	11 (31)	8 (32)	3 (27.3)	
Symptoms				
Nausea	32 (89)	22 (88)	10 (91)	1.00
Vomiting	24 (67)	17 (68)	7 (64)	1.00
Abdominal pain	13 (36)	9 (36)	4 (36)	1.00
Early satiety	12 (33)	11 (44)	1 (9.1)	0.059
Weight loss	8 (22)	4 (16)	4 (36)	0.21
Bloating/distention	8 (22)	5 (20)	3 (27)	0.68
Diarrhea	9 (25)	6 (24)	3 (27)	1.00
Constipation	3 (8.3)	2 (8.0)	1 (9.1)	1.00
Decreased appetite/anorexia	4 (11)	3 (12)	1 (9.1)	1.00
Belching	1 (2.8)	1 (4.0)	0 (0.0)	1.00
Diagnosis				
Gastroparesis	23 (64)	13 (52)	10 (91)	0.031
Cyclic vomiting syndrome	2 (5.6)	2 (8.0)	0 (0.0)	1.00
IBS	3 (8.3)	0 (0.0)	3 (27)	0.023
SIBO	5 (14)	3 (12)	2 (18)	0.63
Malignancy	0 (0.0)	0 (0.0)	0 (0.0)	0.63
GERD	5 (14)	5 (20)	0 (0.0)	0.30
Dumping syndrome	1 (2.8)	0 (0.0)	1 (9.1)	0.31
Unspecified	5 (14)	5 (20)	0 (0.0)	0.30

SIBO = small intestinal bacterial overgrowth; GERD = gastroesophageal reflux disease.

Except for age, data are numbers followed by percentage in parentheses; n = 36 patients total.

transit is less commonly encountered. Criteria for diagnosing rapid small-bowel transit remain poorly defined; however, current definitions include visually identifying early cecal filling (≥10% of administered activity in the cecum) in less than 70 min (reference range, 72–392 min for cecal arrival in the dual-isotope meal method) (*8*,*22*).

CONCLUSION

This study demonstrated that administration of an LNM in cases of equivocal SBTS results helps allow image interpretation by delineating the TIR and the cecum or colon. There was a significant decrease in the number of equivocal SBTS cases after administration of an LNM at 6 h, with most cases converting to a definitive result. Gastroparesis and IBS were associated with a poor response to an LNM, but the clinical significance remains in question, and further study will be required to determine whether such patients have both a gastric and a small-bowel transit disorder.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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