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THE UTILITY OF ADDING A LIQUID NUTRIENT MEAL TO AID INTERPRETATION OF SMALL BOWEL TRANSIT SCINTIGRAPHY

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ABSTRACT

Small bowel transit scintigraphy (SBTS) evaluates the accumulation of a radiolabeled meal in the terminal ileal reservoir (TIR) 6 hours after meal ingestion. The TIR may be difficult to determine as 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 a liquid nutrient meal (LNM) at 6 hours can promote movement of the radiolabeled meal to aid in the interpretation of SBTS. **Methods**: This retrospective study reviewed 117 SBTS from 2/2017 to 9/2019. Patients were fed a standardized mixed radiolabeled solid- liquid meal for gastric emptying with SBTS according to SNMMI Practice Guidelines. Additional LNM was given at 6 hr, and post-LNM images were obtained at least 20 minutes after the LNM. Two board-certified nuclear medicine physicians independently evaluated all images at 6 hours as equivocal or diagnostic. **Results**: Of the 117 patients (71.8% female, median age 42.0) undergoing SBTS, 37 were equivocal cases at 6 hours pre-LNM (31.6%, 95% CI=23.3%-40.9%) compared to 12 equivocal cases post-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 LNM administration while 11 (30.6%, 95% CI=16.4%-48.1%) remained equivocal, and 1 showed rapid transit. In patients with gastroparesis, only 13/23 (57%) responded to LMN, while 0/3 IBS patients responded. **Conclusion:** The number of equivocal SBTS cases decreased after administration of a LNM at 6 hours, converting to a definitive result. This suggests that with use of a LNM a majority of patients can complete SBTS in one day without the need for repeat imaging at 24 hours. Administering a LNM appears to be less effective for patients with gastric disorders. However, the clinical significance remains to be explored and it is unclear if these patients have both a gastric and small bowel disorder, hence reducing any motility-promoting effect of the LNM.

KEYWORDS: small bowel transit scintigraphy; liquid nutrient meal, gastrointestinal dysmotility; gastroparesis; irritable bowel syndrome

INTRODUCTION

Small bowel dysmotility can be seen in an array of gastrointestinal tract disorders, including but not limited to irritable bowel syndrome, chronic idiopathic intestinal pseudo-obstruction, 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, and/or vomiting (*2,3,5*). Given these non-specific symptoms, differentiating between upper and lower GI tract dysfunction in patients with suspected motility disorders can be challenging for clinicians. Evaluating small bowel motility may provide diagnostic information (*6*).

Gastric emptying scintigraphy (GES) is recognized as the "gold standard" for analyzing gastric motility, as it utilizes a physiologic meal to provide accurate quantification of the emptying of a meal from the stomach over the course of 4 hours (*2*). Small bowel transit scintigraphy (SBTS) is increasingly being utilized as a continuation of the standard GES. 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 ileum (*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 a prior normal GES. Current guidelines for SBTS require measurement of the radiolabeled meal 6 hours after meal ingestion of a standardized mixed solid-liquid radiolabeled meal (*8*). SBTS is considered normal if > 40% of administered solid-liquid meal activity has progressed into the terminal ileal reservoir (TIR) and /or progressed into the cecum/ascending colon at 6 hours (*9*). Accurate identification of the TIR can be difficult to identify due to the lack of anatomical information available in scintigraphic images, rendering the study result equivocal at 6 hours. Additionally, correlation with other anatomic imaging such as abdominal radiographs or computed tomography is not always available. As such, patients with an

equivocal study often need to return at 24 hours 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 terminal ileum to the colon in bolus movements that correspond to ileal contractions (*10*). Following 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 high caloric liquid nutrient meal (LNM) at 6 hours can stimulate progression of the radiolabeled meal to help identify loops of distal small bowel and the TIR location and/or potential transit into the colon. We additionally correlated patients' clinical symptoms and diagnoses to the response of the administration of a LNM to determine if certain conditions are more predictive of a positive or equivocal response to the LNM.

MATERIALS AND METHODS

Study Design

Our institutional review board (Temple University Lewis Katz School of Medicine) 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 IRB regulations and presented to the readers in random order with a delay of at least 6 months from the time of the original clinical study to help prevent any unblinding.

Patients were fed a standardized mixed solid plus liquid meal as specified in the SNMMI Guidelines (*8*). The solid meal radiolabeled egg white was labeled with approximately 500 μCi of Tc-99m sulfur colloid. The liquid portion of the meal consisted of approximately 125 μC of In-111 DTPA in 6 oz of water administered with the egg white meal sandwich. The unlabeled portion of the meal

consisted of two pieces of white bread toast plus jam (30 g). Images of the abdomen were then obtained in both anterior and posterior projections for 6 hours after meal ingestion to record SBT. From these images, liquid gastric emptying at 1 hour and SBT at 6 hours were measured.

Upon completion of the study at 6 hours, patients included in this study were all patients who received a LNM with repeat imaging 20 minutes afterwards. The LNM used is a commercially available 8 fluid oz bottle containing 360 kcal, 14 g protein, 45 g carbohydrates, 3 g fiber, 22 g sugar, and 14 g fat. All patients received a LNM during their SBTS at the 6-hour time-point, regardless of the result of the SBTS to reduce variations and differences in practice between clinicians. All results were analyzed after all data were collected.

Patient demographic information at the time of the SBTS was obtained, including age, sex, race, symptoms, and final diagnoses from the patients' electronic medical record. All images were independently reviewed by two board-certified nuclear medicine physicians. Original interpretation of SBTS images was recorded as normal (N), abnormal delayed SBT (A), or equivocal (E) based on 6-hour images before (pre-LNM) and after (post-LNM) the supplemental meal. SBTS is considered normal if > 40% of administered liquid meal activity has progressed into the terminal ileal reservoir (TIR) and/or passed into the cecum/ascending colon at 6 hours (*9*).

Representative images are shown in **Figure 1 to 4**. Figure 1 demonstrates a normal SBTS, in which there is an accumulation of activity within the TIR and into the colon. Figure 2 describes an abnormal study, 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, which responded to LNM. In this case, the pre-LNM images showed some progression of activity into the right lower quadrant but it is unclear whether this represent filling of the TIR. Following the LNM there is clear progression of activity

from the right lower collection into the cecum and ascending colon, confirming the location of the TIR prior to LNM administration. For a study to be considered changed from an equivocal to definitive finding of normal or delayed SBT, the reader had to be certain that focal activity in the right lower quadrant progressed directly into the cecum/ascending colon or questionable loops of non-focal small bowel activity all progressed further into a single focal area consistent with the TIR.

The readers' interpretations of pre-LNM and post-LNM images were obtained all at the same time. **Supplemental Table S1** shows a frequency count of all combinations of pre-LNM results recorded by the two readers. Only cases that were mutually agreed upon by the two readers at the pre-LNM time point were included in the main analysis, as shown in **Supplemental Figure S1**. This criterion prevents the introduction of bias through reviewing images repeatedly. Only disagreements of the post-LNM images between the two readers were adjudicated by a third independent board-certified nuclear medicine physician (the adjudicator). Cases with rapid small bowel transit were excluded as these patients are not expected to respond to LMN's stimulating effect.

The readers were blinded to all clinical data. The readers' interpretation of the images for this trial occurred greater than 6 months after the initial study was performed. This helped to ensure that the readers carried no prior clinical biases and removed the interpretation/selection process from the clinical practice. All three readers were blinded to the primary and secondary outcomes until all data collection was complete.

The primary endpoint was the proportion of patients who initially had inconclusive identification of the TIR and transition to colon at 6 hours that changed to a definitive diagnosis after the administration of a LNM. Secondary endpoints included the comparison of clinical diagnoses of patients who responded to a LNM to those who did not as well as a subset analysis of factors that may predict a response to a LNM.

Statistical Analysis

Descriptive summary statistics are presented as means with standard deviations or medians with ranges for continuous variables and frequencies with percentages for categorical variables. The Pearson-Clopper exact method was used to calculate binomial confidence intervals for proportions. The Fisher exact test was employed to test for associations between two categorical variables, whereas the Wilcoxon rank test was used to determine associations of continuous covariates with a response outcome. Collected data were managed in Microsoft Excel®. Statistical data analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

RESULTS

Patient Characteristics

Between February 1, 2017 and September 1, 2019, SBTS were performed on 117 patients [71.8% (84/117) female, 83.8% (98/117) Caucasian, median age 47, age range 19-70 years old] at our institution. Patient demographics are shown in **Table 1.** One case with rapid SBT was encountered and was removed from the cohort due to early rapid transit to the colon such that administration of the LNM was not a consideration.

Enhancing Effect of a Liquid Nutrient Meal on Equivocal Cases

Of the 117 cases, 37 had concordant equivocal results pre-LNM and 80 cases had definitive diagnostic results of normal or delayed SBT. **Table 2** summarizes the results of these cases. The percentage of equivocal cases decreased from 31.6% (37/117) (95% CI=23.3%-40.9%) pre-LNM to 10.3% (12/117) (95% CI=5.4%-17.2%) post-LNM. For 25 of the 37 patients, the LNM helped with the interpretation of the study; 16 were normal SBT and 9 were delayed SBT. Of the 37 equivocal pre-LNM cases, 1 case was removed from the cohort after adjudication, as it demonstrated rapid transit to the colon.

Therefore, only 36 cases completed subsequent analysis. **Supplemental Table S2** describes the frequency of pre-LNM equivocal cases that yielded a definitive result after administration of a LNM. Of the remaining 36 equivocal cases, 25 cases (69.4% (25/36), 95% CI= 51.9%-83.7%) had a definitive result post-LNM (16 cases were normal and 9 cases were abnormal), while 11 cases (30.6% (11/36), 95% CI= 16.4%-48.1%) remained equivocal. Only 4 of the 11 cases had a 24-hour study completed the following day.

Clinical Characteristics Correlating to the Effect of a Liquid Nutrient Meal

To further understand the clinical utility of administering a LNM, a comparison of clinical characteristics was made between cases that responded to a LNM (i.e., produced a definitive result post-LNM) and those that remained equivocal post-LNM. **Table 3** illustrates these comparisons of basic demographics, symptoms, and subsequent diagnoses. Gastroparesis and IBS (irritable bowel syndrome) were both noted to be significantly associated with a negative response to a LNM when comparing equivocal cases to the definitive counterpart, 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 post-LNM [9.1% (1/11) vs. 44.0% (11/25)]; however, it did not reach statistical significance with a p-value of 0.059.

DISCUSSION

The aim of this study was to examine whether the administration of a LNM helped facilitate visualization of the TIR and colonic transit in equivocal SBTS at the standard 6-hour time point. Our results show that the number of equivocal SBTS studies was significantly decreased after the administration of a LNM at 6 hours, with a majority of cases converting to a definitive result. This 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 hours. Difficulty in reliably identifying anatomic landmarks of where the TIR and cecum are located as well as the time consuming nature of SBTS are often cited as significant disadvantages to SBTS (*11,12*). However, the effect of a LNM on promoting the 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 hours. This suggests that when imaging findings are equivocal at 6 hours, administration of a LNM should be considered as a routine procedure.

In assessing the clinical characteristics correlating to the effect of a LNM, it was noted that gastroparesis and IBS were predictive of a negative response to the LNM. However, there are several distinct etiologies of gastroparesis including diabetic, post-surgical, and idiopathic (*13*). As the various etiologies of gastroparesis were grouped together, this 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, a negative response to a 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*). All subgroups of IBS were grouped together in this study, which may account for the overall observed negative response to a LNM among IBS patients within our cohort. From a clinical perspective, perhaps the patients with gastric disorders have both gastric and small bowel dysfunction, and the administration of a LNM was unable to stimulate any additional motility as these patients are symptomatic. Hence, the interpretation of the effect of using a LNM in patients with gastric disorders remains unclear and warrants further study.

There are several study limitations that warrant further discussion. Of note, the time interval between LNM administration and obtaining post-LNM images was reviewed to ensure no confounding effect. The study standardization required at least a 20-minute wait period after the administration of a LNM and capturing the first post-LNM image. Upon review, some images were obtained <20 minutes

after the administration of a LNM. If post-LNM images were obtained too soon, one would expect that there may be inadequate time to exert a pro-motility effect. On the contrary, our results still demonstrated that the number of equivocal SBTS converting to a definitive result remained significant regardless of the potential for a shortened interval for post-LNM images.

Another study limitation is inter-observer variability. Inter-observer variability is not limited to SBTS but is in fact well documented in scintigraphy and in the field of radiology in general (*16-18*).A post hoc analysis revealed the concordance rate between the two primary readers to be 55% (65/117) among pre-LNM results, which is similar to what has been documented in the literature (*16,17*). We also recognize that in the absence of a true "gold standard" for the two primary readers' discordant readings, we have used a third reader adjudication. While not a perfect gold standard, such adjudication is accepted in clinical trials by regulatory agencies such as the Food and Drug Administration (*19*).

As only four patients underwent confirmatory 24-hour studies, conclusions on the value of 24-hour imaging cannot be drawn. A contributing factor limiting our utilization of 24 hour imaging is that it is typical at our institution that patients undergoing SBTS are scheduled for a hydrogen breath test on day following SBTS. Repeat imaging at 24 hours 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 not having a confirmatory study to compare against, our result still showed a near 70% rate of response to LNM, suggesting its utilization in clinical practice.

Our study analysis was directed primarily towards evaluation of delayed SBT. Rapid SBT is less commonly encountered. Criteria for diagnosing rapid SBT remains poorly defined; however, current definitions include visually identifying early cecal filling (≥10% of administered activity in the cecum) in less than 70 minutes (reference range: 72-392 minutes for cecal arrival in the dual-isotope meal method) (*8,22*).

CONCLUSION

In conclusion, this study demonstrates that a LNM administered for equivocal SBTS is helpful for delineating the terminal ileum and cecum/colon anatomy to allow interpretation of the study. There was a significant decrease in the number of equivocal SBTS after the administration of a LNM at 6 hours, with a majority of cases converting to a definitive result. Gastroparesis and IBS were both noted to be associated with a poor response to a LNM, but the clinical significance remains in question and will require further study to determine if these patients have both a gastric and small bowel transit disorder.

DISCLOSURES:

All authors declare no conflict of interest.

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None.

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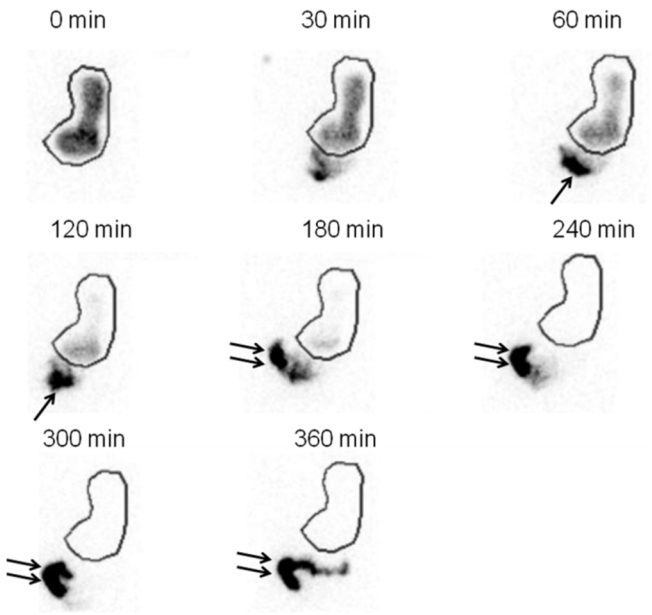


FIGURE 1. 20 year old male with nausea and vomiting, underwent sequential gastric emptying images, which showed normal small bowel transit. There is normal progressive filling of the terminal ileum reservoir (single arrows) and then early progression into the cecum and colon (double arrows) (anterior views). More than 40% of the total activity has progress from the terminal ileum reservoir into the colon by 360 minutes.

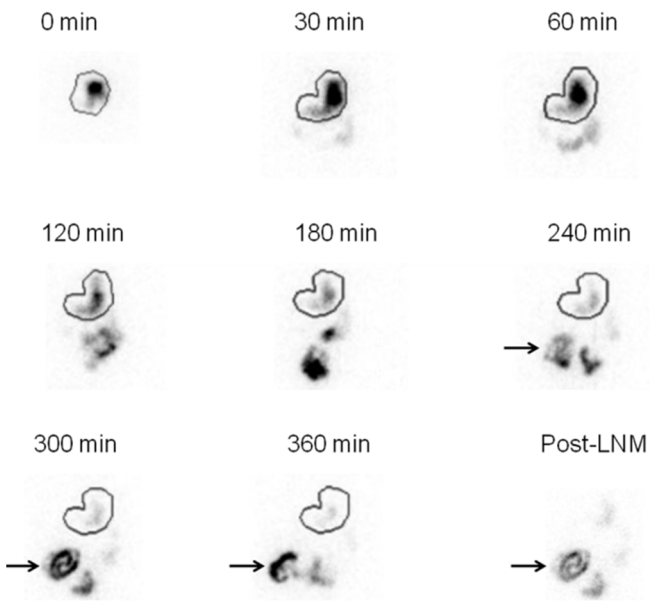


FIGURE 2. 30 year old male presented with nausea, vomiting, abdominal pain and weight loss, who underwent SBTS, found to have delayed or abnormal small bowel transit (anterior views). In contrast to Figure 1, there is persistent and diffuse activity within loops of proximal small bowel, and no accumulation of activity in the terminal ileum reservoir (arrows) by 360min. There was no change in the pattern of more proximal loops of small bowel after the administration of a liquid nutrient meal (LNM).

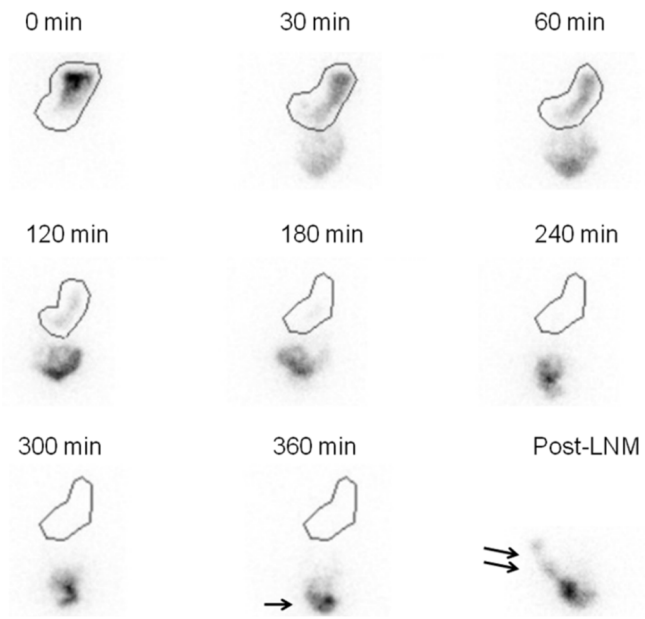


FIGURE 3. 27 year old female presented with nausea, diarrhea, bloating and abdominal distention, found to have equivocal small bowel transit study but confirmation of terminal ileum/colon localization following administration of LNM (anterior views). There is progression of activity into the right lower quadrant but it is unclear this represent filling of the terminal ileum by 360min (single arrow). Following the LNM, however, the anatomy is more clearly defined showing normal progression of activity from the terminal ileum into the colon (double arrows)

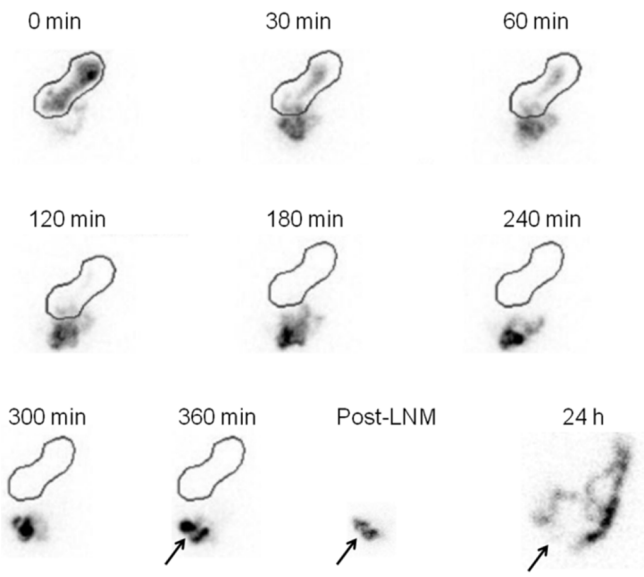


FIGURE 4. 17 year old male with abdominal pain and early satiety, found to have equivocal small bowel transit at 6 hours (anterior views). While there is an accumulation of activity in the right lower quadrant at 6hr (arrow), this does not clearly progress into the cecum or ascending colon following the LNM. A 24-hour image, however, helps to better define the anatomy and shows the site of build up in the right lower quadrant (arrow) was the terminal ileum with progression of activity into the ascending, transverse, and descending colon, confirming normal small bowel transit.

TABLES

Table 1. Baseline characteristics of all studied patients.

Baseline characteristics	All patients (N=117)
Age, median [19]	42 (17-81)
Sex	
Male, N(%)	33 (28.2)
Female, N(%)	84 (71.8)
Race, N(%)	
White	98 (83.8)
Black	8 (6.8)
Hispanics	10 (8.5)
Mixed	1 (0.9)
BMI, N (%)	
≤19	15 (12.8)
20-24	32 (27.4)
25-29	37 (31.6)
≥30	33 (28.2)
Symptoms, N(%)	
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, N(%)	
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)

Abbreviations: BMI, body mass index; IBS, irritable bowel syndrome; SIBO, small intestinal bacterial overgrowth; GERD, gastroesophageal reflux disease;

TABLE 1. Patient demographics and clinical information.

Table 2. Frequency and percentages of SBTS result before and after administration of LNM. Thirty seven equivocal cases received a LNM to help aid in the localization of the TIR/cecum.

N=117 cases	**Pre-LNM, N(%)**	**Post-LNM, N(%)**
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)*

TABLE 2. Proportion of cases that were assigned as equivocal or definitive results. Definitive results further divide in to normal small bowel motility or abnormal small bowel motility. Administration of a liquid nutrient meal reduced the percentage of equivocal cases from 31.6% (95% CI 23.3%-40.9%) to 10.3% (95% CI 5.4%-17.2%). CI = confidence interval.

Table 3. Baseline characteristics and their comparisons based on responses to LNM for all equivocal cases where a LNM was indicated (n=36)

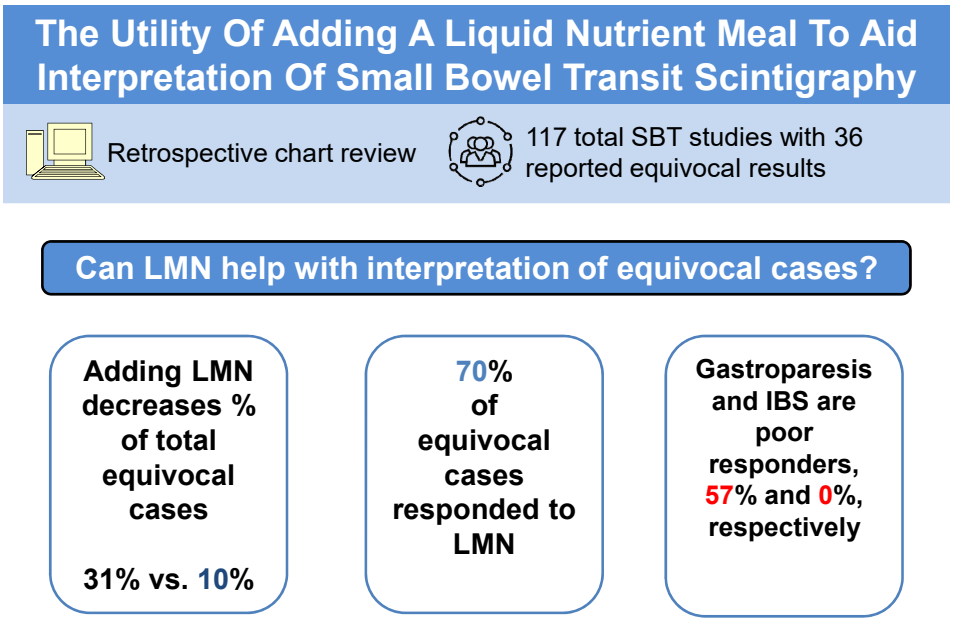
Baseline characteristics	All (N=36)	Definitive (N=25)	Equivocal (N=11)	P-value
Age, median (range)	40 (19-70)	40 (19-70)	35 (20-69)	0.52
Sex				
Male, N(%)	6 (17)	5 (20)	1 (9.1)	0.64
Female, N(%)	30 (83)	20 (80)	10 (91)	
Race, N(%)				
White	29 (81)	21 (84)	8 (73)	0.096
Black	3 (8.3)	3 (12)	0 (0.0)	
Hispanics	3 (8.3)	1 (4.0)	2 (18)	
Mixed	1 (2.8)	0 (0.0)	1 (9.1)	
BMI, N (%)				
≤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, N(%)				
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, N(%)				
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

Wilcoxon sign test was used for continuous variables. Fisher's exact test used for categorial variables.

Abbreviations: BMI, body mass index; IBS, irritable bowel syndrome; SIBO, small intestinal bacterial overgrowth; GERD, gastroesophageal reflux disease;

TABLE 3. Subset analysis of all equivocal cases where a LNM was indicated. Of the 36 cases, 25 yielded definitive results after LNM was given, while 11 cases remained equivocal. Wilcoxon rank test was used to determine p-value for continuous variables, while Fisher's exact test used for categorical variables. A diagnosis of either gastroparesis or irritable bowel syndrome is significantly associated with equivocal results after LNM (p=0.031, 0.023, respectively). The symptom of early satiety correlates to yielding a definitive result after giving LNM, however, p=0.059

GRAPHICAL ABSTRACT



SUPPLEMENTAL MATERIALS

Supplemental Table S1. Frequency table of concordance and discordance between reader 1 and reader 2. Due to the large variation between the two readers and to reduce any possible bias, only mutually agreed upon equivocal cases were selected for further analyses. *Abbreviations: A, abnormal; E, equivocal; N, normal.*

Pre_LNM_Reader1	*Pre_LNM_Reader2*	*Frequency*	*Percent*
--	*A*	1	0.85
A	*A*	3	2.54
A	*N*	1	0.85
E	--	1	0.85
E	*A*	13	11.02
E	***E***	***37***	***31.36***
E	*N*	16	13.56
N	*A*	4	3.39
N	*E*	17	14.41
N	*N*	25	21.19

Supplemental Table S2. Frequency table of final result for all equivocal cases that received LNM. Of the 36 cases, 11 remained equivocal after LNM, while 25 cases produced a definitive result.

Abbreviations: A, abnormal; E, equivocal; N, normal.

PreLNM Result	*PostLNM Final Read*	*PostLNMResult*	*Frequency*	*Percent*	*Cumulative Frequency*	*Cumulative Percent*
Definitive	LNM not indicated		82	69.49	82	69.49
Equivocal	*A*	*Definitive*	9	7.63	91	77.12
Equivocal	*E*	*Equivocal*	11	9.32	102	86.44
Equivocal	*N*	*Definitive*	16	13.56	118	100.00

Supplemental Figure S1. Demonstrates the series of criteria used to filter cases for subsequent analyses.