Small Bowel Transit Scintigraphy in Children With Pediatric Intestinal Pseudo-Obstruction

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INTRODUCTION: **Objective evidence of small intestinal dysmotility is a key criterion for the diagnosis of pediatric intestinal pseudo-obstruction (PIPO). Small bowel scintigraphy (SBS) allows for objective measurement of small bowel transit (SBT), but limited data are available in children. We aimed to evaluate the utility of SBS in children suspected of gastrointestinal dysmotility.**

METHODS: **Patients undergoing gastric emptying studies for suspected foregut dysmotility, including PIPO, from 2016 to 2022 at 2 tertiary children's hospitals were recruited to an extended protocol of gastric emptying studies to allow for assessment of SBT. PIPO was classified based on antroduodenal manometry (ADM). SBT was compared between PIPO and non-PIPO patients. Scintigraphic parameters were assessed and correlated against ADM scores.**

RESULTS: **Fifty-nine patients (16 PIPO and 43 non-PIPO diagnoses) were included. SBS was performed with liquid and solid meals in 40 and 26 patients, respectively. As compared to the non-PIPO group, PIPO patients had a significantly lower median percentage of colonic filling at 6 hours, with both liquid (48% vs 83%) and solid tests (5% vs 65%). SBT in PIPO patients with myopathic involvement was significantly slower than in patients with neuropathic PIPO, both for liquid and solid meal. A significant correlation was found between solid SBT and ADM scores ($r = -0.638$, $P = 0.036$).**

DISCUSSION: **SBS provides a practically feasible assessment of small intestinal motility. It shows a potential utility to help diagnose and characterize PIPO. SBS seems most discriminative in PIPO patients with myopathic involvement. Studies in a larger pediatric population and across different ages are required.**

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C980, http://links.lww.com/AJG/C981, http://links.lww.com/AJG/C982, and http://links.lww.com/AJG/C983.

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INTRODUCTION

Small bowel transit (SBT) tests are less-invasive methods for the assessment of small intestinal function, as compared to antroduodenal manometry (ADM) and histopathology from full-thickness intestinal biopsies. They are considered physiologic methods allowing for readout of the time taken for the small bowel to propel its contents (1–4).

Currently, ADM has been used as a tool for assessing small intestinal dysmotility. Although this test has not been standardized in either children or adults, potential enhancements have been observed in the recent years. By using an increased breadth of analysis for various contractile parameters and developing an associated score Great Ormond Street Hospital London ADM Scoring System (GLASS), the diagnosis and subtypes of pediatric intestinal pseudo-obstruction (PIPO) seemed to better correlate with histological findings from full-thickness small intestinal biopsies (5). However, both the insertion of manometric catheter into the small bowel and small bowel full-thickness biopsies may be considered as invasive methods.

Scintigraphic assessment of SBT time allows for direct non-invasive quantitative readout of small intestinal propulsion by

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tracking the progression of an ingested radiopharmaceutical propelled through the intestine (4). In recent recommendations (2), it is suggested as a potential tool to provide objective evidence of small intestinal neuromuscular involvement, one of the key criteria for the diagnosis of PIPO (2). Small bowel scintigraphy (SBS) is usually performed using either a single technetium-99m–labeled liquid test feed alone or a combination of solid and liquid using both technetium-99m (^{99m}Tc; 6-hour half-life) and indium-111 diethylenetriaminepentaacetic acid (^{111}ln-DTPA; 2.8-day half-life) (6,7). After the ingestion of a standardized radiolabeled meal (orally or through gastrostomy), the percentage of gastric retention and the movement of radiotracer from the stomach to the cecum are obtained at different time intervals. This allows for the determination of gastric emptying and SBT time.

To quantify SBT, several methods have been used (6,8). The terminal ileum filling method is based on the observation that the proximal small bowel has the most rapid transit, with a slower transit into the distal part and the terminal ileum serving as a reservoir (9). Therefore, the activity filling the terminal ileum before it crosses the ileocecal valve into the colon has been suggested to represent SBT.

The simplest scintigraphic approach is to determine the orocecal transit by using the amount of colon filling at 6 hours as an index of SBT. This method has provided good correlation with the hydrogen breath test (10).

Generally, the reference scintigraphic values of the small bowel depend on the measurement method, the radioisotope used, and the type of meal. According to The Society of Nuclear Medicine and Molecular Imaging and European Association of Nuclear Medicine Practice Guidelines, SBT is normal if at 6 hours, more than 40% of administered ^{111}In-DTPA radioactivity has reached either the terminal ileum or colon (6). This definition has been widely used as an index of normal SBT in several studies, particularly in the adult population (11–13).

Despite several studies and guidelines used in adults, there is a lack of normative data on small intestinal scintigraphy in children. In addition, there are limited data on SBS in children with motility disorders, although several studies have been performed in adults (6,7,14). Therefore, this study aimed to evaluate the utility of SBS to help diagnose small bowel dysmotility in children, to identify possible reference values for the diagnosis of PIPO and to correlate findings with ADM, a standard test for small intestinal motility.

METHODS

Patients

All patients included in the study were referred to Great Ormond Street Hospital (GOSH) between January 2016 and December 2022, or to Queensland Children's Hospital (QCH) between January 2019 and December 2022, for further management. The patients underwent investigations of the gastrointestinal (GI) tract for gastric and small intestinal functional or motility disorders as part of their routine clinical care. A detailed description of patient selection, inclusion and exclusion criteria, and diagnostic definition is reported in the Appendix (Supplementary Digital Content 4, http://links.lww.com/AJG/C983).

Ethical considerations

The study protocol was approved by the Institutional Review Board of GOSH and Health Research Authority and Health and Care Research Wales for conduct in the National Health Service by the London-Brent Research Ethics Committee (REC Ref 19/LO/0854). It was also approved by the Human Research Ethics Committee, Children's Health Queensland Hospital and Health Service, Brisbane, Australia (HREC/21/QCHQ/72690).

Small bowel transit

For the gastric emptying studies (GES), the progression of a radiolabeled meal was measured by obtaining sequential scans over 3–4 hours with a dual-head gamma camera. For the liquid test meal, a test feed based on milk or formula was labeled with ^{99m}Tc-nanocolloid; a solid test meal based on egg white on toast or melted cheese on toast or pasta, radiolabeled with ^{99m}Tc-nanocolloid, was ingested. The SBS was performed by acquiring additional images up to 6–8 hours after meal ingestion to follow the movement of the test feed through the small intestine.

To establish the orocecal transit, a region of interest was manually drawn around the expected location of ileocecal valve and/or cecum and any colonic activity measured at 6 hours (Figure 1). A detailed description of scintigraphic method is reported in the Appendix (Supplementary Digital Content 4, http://links.lww.com/AJG/C983).

Antroduodenal manometry

The ADM tracing was analyzed by pediatric neurogastroenterologists as part of standard clinical care. The analysis was mainly based on qualitative characteristics obtained from selected segments of the ADM recording. The final reports from this conventional analysis were collected. Since the enhanced ADM analysis and GLASS score have recently been established, the ADM recordings were anonymized and reanalyzed based on previously published method (5) (Appendix, Supplementary Digital Content 4, http://links.lww.com/AJG/C983). A GLASS score of $\geq$10 was used to discriminate between PIPO and control patients; myopathy was identified by the presence of low amplitude of overall phase 3 contraction (<10 mm Hg) (5). A detailed description of ADM method is presented in the Appendix (Supplementary Digital Content 4, http://links.lww.com/AJG/C983).

RESULTS

Over 6 years, 59 patients (42 from GOSH and 17 controls from QCH) undergoing SBS were included in the study. Based on clinical and/or manometric criteria, 16 children were diagnosed with PIPO (median age of 8.98 years; interquartile range [IQR] 3.45–13.04) and 43 with non-PIPO diagnoses (median age of 11.13 years; IQR 4.44–16.09). There was no significant age difference between the 2 groups (P = 0.213). SBS was performed with liquid and solid test meals in 40 and 26 patients, respectively. Only 7 patients underwent both liquid and solid SBS. Demographic data for all patients are presented in Table 1.

Liquid SBS

Forty patients had SBS performed with a liquid test feed. Based on clinical and/or manometric criteria, 15 were diagnosed with PIPO and the remaining 25 with non-PIPO. The diagnoses in the non-PIPO (control) group included lower GI motility and functional disorders (GIMD) and upper GIMD. Demographic data for patients having liquid SBS are presented in Table 2.

With a liquid test meal, PIPO patients had a significantly lower percentage of radiotracer reaching the colon within 6 hours, as

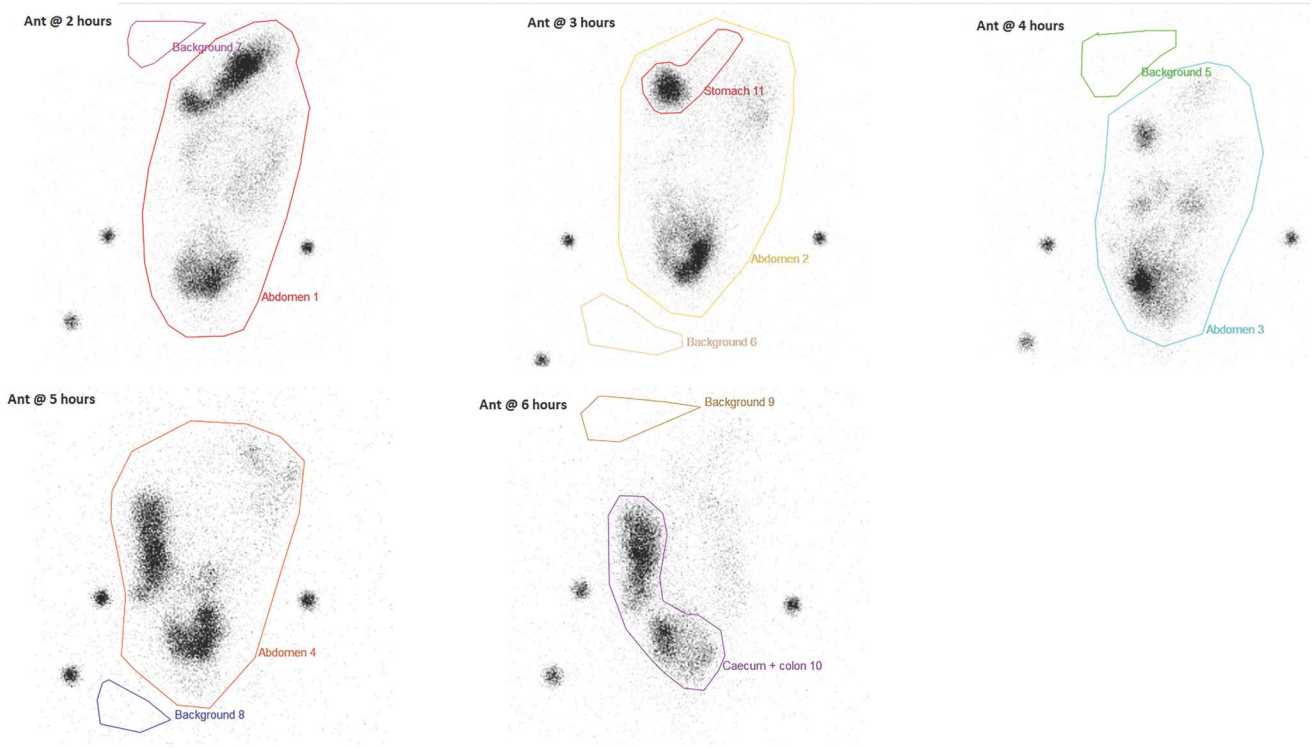

Figure 1. Regions of interest manually drawn (both anterior and posterior view) around the stomach at 3 hours and around the cecum and entire abdomen between 2 and 6 hours

compared to non-PIPO patients (48% vs 83%, $P = 0.005$; Figure 2).

From the receiver operating characteristic analysis, colonic filling of <55% at 6 hours after liquid meal ingestion provided a sensitivity of 68% for the diagnosis of PIPO and specificity of 84%, with an area under the curve of 0.765 ($P = 0.005$). It also provided a positive and negative predictive value of 67% and 80%, respectively.

By using enhanced ADM analysis and the associated GLASS score (5), 15 PIPO patients were classified into 2 groups: neuropathy (n = 12) and neuromyopathy (n = 3). Among these different PIPO subtypes, neuromyopathy had slower SBT compared with neuropathic PIPO and non-PIPO patients (6% vs 52% vs 83%, $P = 0.005$; Figure 3).

As mentioned earlier, the non-PIPO patients included those with both upper and lower GIMD. SBT was not significantly different between patients with and without lower GIMD (73% vs 89%; $P = 0.608$; Supplementary Figure 1A, Supplementary Digital Content 1, http://links.lww.com/AJG/C980). Neuromyopathy had slower SBT compared with neuropathic PIPO and non-PIPO patients without lower GIMD (6% vs 52% vs 73%, $P = 0.016$; Supplementary Figure 1B, Supplementary Digital Content 1, http://links.lww.com/AJG/C980).

Correlation between liquid SBT and ADM. Nine and 15 patients in the non-PIPO and PIPO groups, respectively, underwent both liquid SBS and ADM monitoring. The median interval between liquid SBS and ADM was 6 days (Table 2).

Among 9 non-PIPO patients, 4 had conventional ADM analysis reported as unspecified abnormalities with enhanced ADM scores ≥10. However, they did not fulfill the other criteria for the diagnosis of PIPO. None of the 4 patients had colonic filling of <55% at 6 hours after the liquid meal.

All 15 PIPO patients had enhanced GLASS scores of ≥10. SBT in these patients was slow (colonic filling of <55% at 6 hours) in 10 patients.

When comparing the percentage of colonic filling at 6 hours with enhanced ADM (GLASS) score in 24 patients, there was no significant correlation between SBT of liquid meal and ADM score of manometric abnormalities (Spearman r = −0.266; $P = 0.208$).

Solid SBS

Twenty-six small bowel scintigraphies were performed with a solid test meal. Based on clinical and/or manometric criteria, 5 of 26 patients were diagnosed with PIPO and the remaining 21 with non-PIPO. Demographic data for patients having solid SBS are presented in Table 3.

With a solid test meal, PIPO patients had a significantly slower SBT with the median value of radiotracer accumulation in the cecum at 6 hours of 5% compared with 65% in the non-PIPO group ($P < 0.001$; Figure 4).

The result from the receiver operating characteristic analysis showed that a colonic filling of ≤26% provided a sensitivity of 100% and specificity of 81% for the diagnosis of PIPO (area under the curve = 0.962; $P = 0.002$). It also provided a positive and a negative predictive value of 56% and 100%, respectively.

Correlation between solid SBT and ADM. Based on enhanced ADM analysis (5), 3 PIPO patients were classified as neuropathic and 2 as neuromyopathic. SBT performed with a solid test meal in patients with neuromyopathic PIPO was slower than in those with neuropathic ADM, with a colonic filling of 1.50% (IQR 1–2) at 6 hours, as compared to 8% (IQR 5–26) in neuropathic PIPO ($P = 0.006$; Figure 5). Nine patients had both solid SBS and ADM.

Table 1. Demographic data for all patients including in the study

Characteristics	Non-PIPO patients (n = 43)	PIPO patients (n = 16)	*P* value
Sex, male (%)	18 (41.86)	9 (56.25)	1.000
Age, yr (IQR)	11.13 (4.44–16.09)	8.98 (3.45–13.04)	0.213
Age onset, yr (IQR)	2.00 (0.33–13.01)	1.00 (0.04–4.00)	0.113
Presenting symptoms (%)			
Vomiting	32 (74.42)	16 (100.00)	0.026
Constipation	27 (62.79)	11 (68.75)	0.766
Abdominal pain	27 (62.79)	11 (68.75)	0.766
Feeding intolerance	23 (53.49)	12 (75.00)	0.233
Nausea	22 (51.16)	2 (12.50)	0.008
Weight loss or failure to thrive	15 (34.88)	9 (56.25)	0.152
Abdominal distension	10 (23.26)	11 (68.75)	0.002
Comorbidity (%)			
Preterm	7 (16.28)	2 (12.5)	1.000
History of malrotation	1 (2.33)	3 (18.18)	0.057
Urinary involvement	7 (16.28)	2 (12.50)	1.000
Bowel dilatation	1 (2.33)	4 (25.00)	0.017
Feeding type (%)			<0.001
Oral liquid/solid	23 (53.49)	2 (12.50)	
Liquid enteral	17 (39.53)	5 (31.25)	
Mixed enteral and parenteral nutrition	3 (6.98)	2 (12.5)	
TPN	0 (0)	7 (43.75)	
Investigations (%)			
Liquid SBS	25 (58.14)	15 (93.75)	0.011
Solid SBS	21 (48.84)	5 (31.25)	0.255
Both liquid and solid SBS	3 (6.98)	4 (25.00)	0.078
ADM	12 (27.90)	16 (100.00)	<0.001
Cine MRI	4 (9.30)	4 (25.00)	0.194
Colonic manometry	7 (16.28)	14 (87.50)	<0.001
Colonic dysmotility	4/7 (57.14)	9/14 (64.29)	1.000
Pellet study	5 (11.63)	0 (0)	0.310
Slow transit	1/5 (20.00)	0 (0)	NA
Anorectal manometry	8 (18.60)	12 (75.00)	<0.001
Abnormal ARM	1/8 (12.5)	1/12 (8.33)	1.000
Full-thickness small intestinal biopsies	1 (2.33)	4 (25.00)	0.017

ADM, antroduodenal manometry; ARM, anorectal manometry; IQR, interquartile range; NA, not applicable; PIPO, pediatric intestinal pseudo-obstruction; SBS, small bowel scintigraphy; TPN, total parenteral nutrition.

The median interval between solid SBS and ADM was 34 days (IQR 4–258). When comparing the percentage of colonic filling at 6 hours with ADM (GLASS) score, there was a significant correlation between solid SBT and ADM score (Spearman r = −0.638; $P = 0.036$).

Solid and liquid SBS

Among 59 patients who underwent SBS, 7 patients had the test performed with both liquid and solid meals (3 non-PIPO and 4 PIPO patients). There was no significant correlation between liquid and solid SBT reported by either qualitative ($P = 1.000$ by the Fisher exact test, Supplementary Table 1, Supplementary Digital Content 3, http://links.lww.com/AJG/C982) or quantitative analysis (Spearman r = 0.393, $P = 0.383$).

When comparing parameters from ADM with SBT in 5 patients (Supplementary Table 1, Supplementary Digital Content 3, http://links.lww.com/AJG/C982), no significant correlation was found between either ADM GLASS score, the ADM score of fasting or postprandial period, and the parameters from liquid and solid SBS.

DISCUSSION

Nuclear scintigraphy has been suggested as the most accurate and sensitive method for the physiological measurement of GI transit because the test allows for the observation and quantification of the physiological movement of liquid or solid foods labeled with radiotracer along the GI tract through images taken with a gamma camera (2,6).

Scintigraphy is recommended by the American Neurogastroenterology and Gastrointestinal Motility Society and the European Society of Neurogastroenterology and Motility to determine SBT in patients with suspected diffuse GI motility disorder (15). However, the normal range is vaguely defined in adults, and the test has not been validated in children. Therefore, this study aimed to evaluate the utility of SBS in children suspected of GI dysmotility, including PIPO.

Given the radiation exposure of scintigraphy is related to the activity of the radioisotope ingested with the test feed rather than the imaging duration and considering the short half-life (6 hours) of the radioisotope used to label both the liquid and the solid test feed (^{99m}Tc), we opted to perform the SBS as a continuation of the standard protocol for GES. Hence, the children undergoing GES as part of normal clinical care could have small bowel scintigraphic examination at no additional radiation risk, albeit with modest additional imaging time. Because the stomach and small intestine work together, as per ADM studies, we believed that a combined GES-SBS would provide a better assessment of upper GI transit. For children with PIPO, there is a significant potential utility in collecting data on both the intestinal contractile pattern as well as the bowel transit, to better understand the underlying pathophysiology and identify the treatment option that best targets the pathophysiologic mechanism of the clinical condition. Of note, in this study, the amount of colon filling at 6 hours was used as an index of SBT because the measure of duodenal bulb to cecal time would require a continuous scanning to identify and measure the amount of radiotracers in the duodenal bulb and significantly longer scanning time (>7-8 hours) to follow the tracers until reaching the cecum. This may not be practical for the patients included.

Table 2. Demographic data for studied patients who had liquid SBS

Characteristics	Non-PIPO patients (n = 25)	PIPO patients (n = 15)	*P* value
Sex, male (%)	13 (52.00)	8 (53.33)	1.000
Age, yr (IQR)	7.76 (3.82–14.15)	8.91 (3.18–13.27)	0.967
Age onset of symptoms, yr (IQR)	0.75 (0.33–11.03)	0.75 (0.03–3.34)	0.387
Presenting symptoms and signs (%)			
Vomiting	21 (84.00)	15 (100.00)	0.278
Constipation	16 (64.00)	10 (66.67)	1.000
Abdominal pain	17 (68.00)	10 (66.67)	1.000
Feeding intolerance	19 (76.00)	12 (80.00)	1.000
Abdominal distension	8 (32.00)	10 (66.67)	0.050
Nausea	8 (32.00)	2 (13.33)	0.269
Weight loss or failure to thrive	5 (20.00)	8 (53.33)	0.041
Bowel dilatation on radiography	1 (4.00)	3 (20.00)	0.139
Comorbidity (%)			
Preterm	4 (16.00)	2 (13.33)	1.000
History of malrotation	1 (4.00)	3 (20.00)	0.139
Urinary involvement	6 (24.00)	2 (13.33)	0.686
Diagnosis (%)			<0.001
PIPO	0 (0)	15 (100.00)	<0.001
Lower GIMD	5 (15.63)	9 (60.00)	1.000
Colonic dysmotility	4 (16.00)	9 (60.00)	1.000
Upper GIMD	23 (92.00)	3 (20.00)	<0.001
GERD	7 (28.00)	0 (0)	0.033
Rumination	5 (20.00)	0 (0)	0.137
Gastroparesis	8 (32.00)	3 (20.00)	0.486
CVS	2 (8.00)	0 (0)	0.519
Functional dyspepsia	2 (8.00)	0 (0)	0.519
Functional nausea	1 (4.00)	0 (0)	1.000
Investigations			
Gastric emptying, % (IQR)	9.00 (1.50–24.00)	15.00 (6.00–20.00)	0.378
ADM (%)	9 (36.00)	15 (100.00)	
Conventional ADM			<0.001
Normal/ unspecified	9/9 (100.00)	1/15 (6.67)	
Neuropathy	0 (0)	12/15 (80.00)	
Neuromyopathy	0 (0)	2/15 (13.33)	
Enhanced ADM			0.001
Normal/ unspecified	5/9 (55.56)	0 (0)	
Neuropathy	1/9 (11.11)	12/15 (68.42)	
Neuromyopathy	3/9 (33.33)	3/15 (31.58)	
ADM score	8.00 (6.50–15.00)	15.00 (13.00–16.00)	0.020
Interval between ADM and SBS, d (IQR)	6.00 (1.50–12.00)	6.00 (2.00–28.00)	0.652
Cine MRI (%)	2 (8.00)	4 (26.67)	0.174
Normal/unspecified	2/2 (100.00)	0/4 (0)	0.050
Bowel dilatation	0 (0)	1/4 (25.00)	
Abnormal peristalsis	0 (0)	3/4 (75.00)	
Interval between Cine MRI and SBS, d (IQR)	40.00 (6.00–74.00)	66.00 (11.25–249.00)	0.355
Full-thickness small intestinal biopsies (%)	1 (4.00)	3 (20.00)	0.139
Normal/unspecified	1/1 (100.00)	1/3 (33.33)	
Abnormal	0 (0)	1/3 (33.33)	
Not available	0 (0)	1/3 (33.33)	
Interval between histology and SBS, d (IQR)	1,447.00	1,086.00 (47.00–1,247.00)	0.180
Pellet study (%)	2 (4.65)	0	0.519
Slow transit	1 (2.33)	—	NA
Interval between pellet study and SBS, d (IQR)	165.50 (8.00–323.00)	—	NA
Colonic manometry (%)	6 (13.95)	13 (81.25)	<0.001
Colonic dysmotility	4 (9.30)	9 (56.25)	1.000
Interval between CM and SBS, d (IQR)	4.00 (2.75–21.75)	10.00 (3.50–152.50)	0.233
Anorectal manometry (%)	6 (13.95)	11 (68.75)	0.003
Abnormal ARM	0	1 (6.25)	1.000
Interval between ARM and SBS, d (IQR)	4.50 (2.75–19.00)	10.00 (4.00–40.00)	0.363
Feeding type (%)			0.005
Oral liquid/solid	7 (28.00)	2 (13.33)	
Liquid enteral	16 (64.00)	5 (33.33)	
Mixed enteral and parenteral nutrition	2 (8.00)	2 (13.33)	
TPN	0 (0)	6 (40.00)	

ADM, antroduodenal manometry; ARM, anorectal manometry; CM, colonic manometry; CVS, cyclic vomiting syndrome; GIMD, gastrointestinal motility and functional disorders; GERD, gastroesophageal reflux disease; IQR, interquartile range; NA, not applicable; PIPO, pediatric intestinal pseudo-obstruction; SBS, small bowel scintigraphy; TPN, total parenteral nutrition.

In the cohort of 59 patients, most patients underwent liquid SBS, given they presented with vomiting and feeding intolerance to solids. In addition, most PIPO patients were PN-dependent; only ~10% were able to feed orally. Although SBS performed with liquids may be less physiologic than solids, it was the form of feed tolerated by all patients in the study and therefore provided the only means of a valid comparison between patients on oral feeds and those who were not tolerant to solid meals.

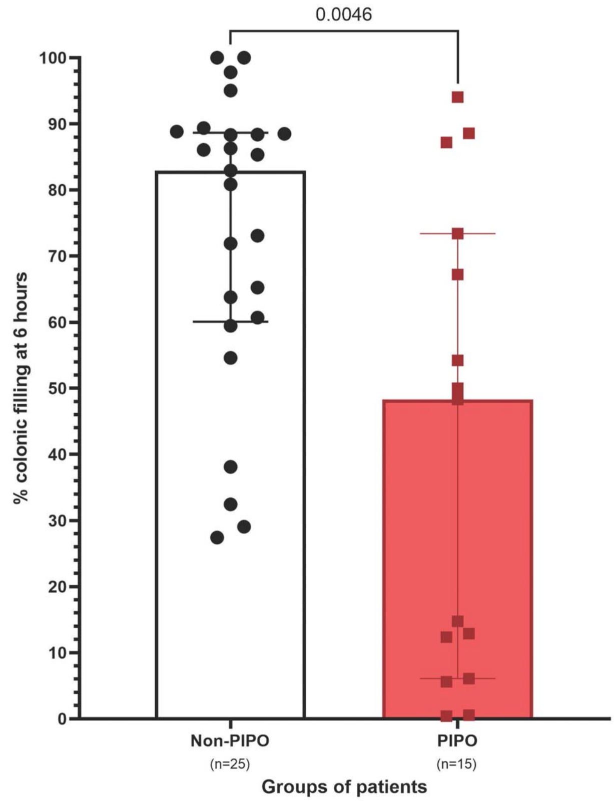

Figure 2. The percentage of colonic filling at 6 hours after liquid meal ingestion in 25 non-PIPO and 15 PIPO patients. PIPO, pediatric intestinal pseudo-obstruction.

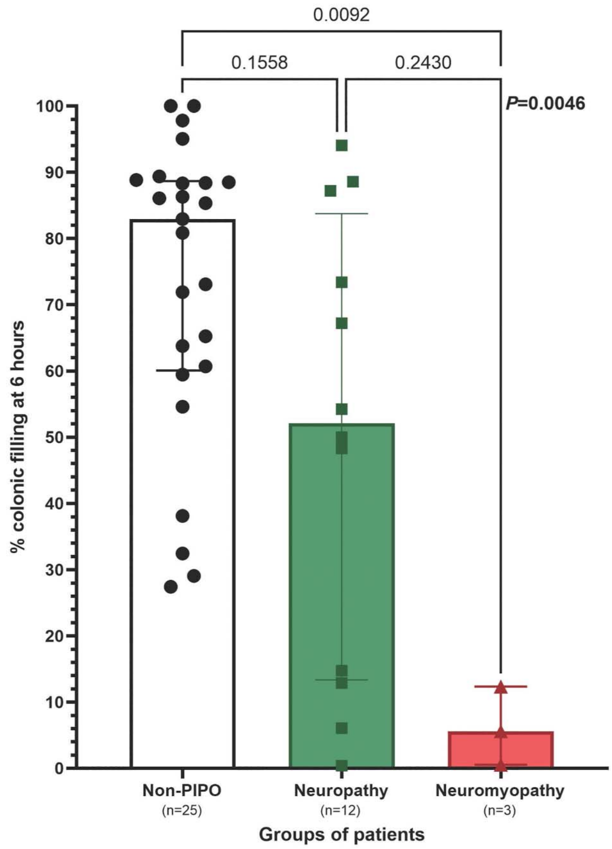

Figure 3. The colonic filling at 6 hours after liquid meal ingestion in controls and patients with different subtypes of PIPO, identified by enhanced antroduodenal manometry analysis. PIPO, pediatric intestinal pseudo-obstruction.

All 16 PIPO patients were diagnosed based on at least 2 of the 4 recommended criteria for the diagnosis of PIPO (2). All patients underwent ADM, and their tracings were analyzed using enhanced analysis and GLASS scores (5). Our earlier study reported that GLASS scores of ≥10 could differentiate PIPO from non-PIPO patients and a higher score represented more severe neuropathic features. In keeping with this, all PIPO patients in this study had GLASS scores of ≥10 (5). Interestingly, 5 of 43 non-PIPO patients had GLASS scores of ≥10, but did not meet criteria for PIPO diagnosis (3 with constipation from colonic dysmotility and 2 with gastroparesis). It is known that constipation and colonic dysmotility can affect small intestinal contractile patterns (16). Furthermore, given the GLASS scores are based on different contractile parameters including the antral response to test feeds (5), patients with gastroparesis might have slightly elevated scores. There was, however, no significant differences in SBT between non-PIPO patients diagnosed with and without lower GIMD. This finding was consistent with previously reported results that constipation did not change the transit pattern of the small intestine (17,18).

In the non-PIPO patients who had liquid SBS, the median percentage of the colonic filling (83%) was higher than the cutoff value (60%–70%), defined in the adult population (6,13). However, this figure was reduced to 72% when excluding the non-PIPO patients with lower GIMD. Of the 20 patients diagnosed with upper GIMD, 25% had prolonged SBT with <55% of test feed reaching the cecum by 6 hours. This is in keeping with a previous study by Maurer et al, where 19% of patients presenting with symptoms of upper GIMD had delayed SBT (13).

We accept that patients presenting with symptoms suggestive of GI dysmotility may not be comparable with healthy children. It is well known that justification for research studies involving ionizing radiations in healthy children is strictly regulated. Although GES and SBS are believed to be noninvasive procedures, there remains concern regarding the risk of ionizing radiation exposure in medical investigations (0.2–0.3 mSv). Also, the patients need to be scanned every hour for at least 6–8 hours to complete the study. Therefore, children diagnosed with GIMD, who required GES as part of their clinical care, were recruited in the study.

As compared to non-PIPO patients, SBT in the PIPO group was significantly prolonged, particularly in those who had myopathic involvement on ADM. The delayed SBT, particularly in PIPO patients with myopathic features, was consistent with findings from previous studies (19–21). In addition, Greydanus et al noted different patterns of bolus transit through the small bowel and ileocolonic bolus transfer among the study groups. Patients with myopathic intestinal pseudo-obstruction showed impaired colonic filling or prolonged ileocolonic bolus transfer, whereas patients with neuropathic small bowel had a similar pattern of bolus transfer to healthy controls but delayed initial cecal arrival time for 10% of the radiotracer (T10%) (21).

For solid SBS, the percentage of solid meal reaching the colon at 6 hours was smaller than with the test performed with liquids. Within the non-PIPO group, the median colonic filling at 6 hours was slower than in those with a liquid feed. It is unclear why there was a difference in the percentage of tracer reaching the colon

Table 3. Demographic data for studied patients who had solid SBS

Characteristics	Non-PIPO patients (n = 21)	PIPO patients (n = 5)	*P* value
Sex, male (%)	6 (28.57)	2 (40.00)	0.628
Age, yr (IQR)	15.79 (9.19–16.46)	7.74 (5.94–9.73)	0.029
Age onset of symptoms, yr (IQR)	11.22 (0.94–14.47)	1.00 (0.25–5.03)	0.048
Diagnosis (%)			
PIPO	0 (0)	5 (100.00)	<0.001
Lower GIMD			
Colonic dysmotility	0 (0)	3 (60.00)	0.200
Upper GIMD	21 (100.00)	1 (20.00)	<0.001
GERD	4 (19.05)	0 (0)	0.555
Rumination	3 (14.29)	0 (0)	1.000
Gastroparesis	10 (47.62)	1 (20.00)	0.356
Functional dyspepsia	3 (14.29)	0 (0)	1.000
Functional nausea	2 (9.52)	0 (0)	1.000
Others	3 (14.29)	0 (0)	1.000
Investigations			
Gastric emptying, % (IQR)	6.00 (1.00–22.50)	4.00 (1.00–14.50)	0.530
ADM (%)	4 (19.05)	5 (100.00)	
Conventional ADM			0.008
Normal/ unspecified	4/4 (100.00)	0 (0)	
Neuropathy	0 (0)	5/5 (100.00)	
Enhanced ADM			0.051
Normal/ unspecified	3/4 (75)	0 (0)	
Neuropathy	1/4 (25)	3/5 (60.00)	
Neuromyopathy	0 (0)	2/5 (40.00)	
ADM score	7.50 (6.25–10.25)	16.00 (14.00–23.50)	0.014
Interval between ADM and SBS, d (IQR)	118.00 (3.50–273.75)	34.00 (4.00–166.00)	0.806
Cine MRI (%)	3 (14.29)	2 (40.00)	0.236
Normal/ unspecified	3/3 (100.00)	0 (0)	
Abnormal peristalsis	0 (0)	2/2 (100.00)	
Interval between cine MRI and SBS, d (IQR)	48.00 (48.00–314.00)	715.00 (289.00–1,141.00)	0.236
Full-thickness small intestinal biopsies (%)	0 (0)	1 (20.00)	0.192
Normal/ unspecified	0 (0)	0 (0)	
Abnormal	0 (0)	1/1 (100.00)	
Interval between histology and SBS, d (IQR)	—	198.00	NA
Pellet study (%)	4 (19.05)	0 (0)	0.555
Slow transit	0/4 (0)	—	NA
Interval between pellet study and SBS, d (IQR)	304.50 (88.75–890.00)	—	NA
Colonic manometry (%)	2 (9.52)	4 (80.00)	0.005
Colonic dysmotility	0 (0)	3/4 (75.00)	0.400
Interval between CM and SBS, d (IQR)	37.00 (2.00–72.00)	6.50 (1.50–32.50)	0.643
Anorectal manometry (%)	3 (14.29)	4 (80.00)	0.010
Abnormal ARM	1 (4.76)	0 (0)	0.429
Interval between ARM and SBS, d (IQR)	10.00 (3.00–613.00)	10.00 (3.25–32.50)	0.714
Feeding type (%)			0.011
Oral liquid/solid	18 (85.71)	2 (40.00)	
Liquid enteral	1 (0)	1 (20.00)	
Mixed enteral and parenteral nutrition	2 (9.52)	0 (0)	
TPN	0 (0)	2 (40.00)	

ADM, antroduodenal manometry; ARM, anorectal manometry; CM, colonic manometry; GIMD, gastrointestinal motility and functional disorders; GERD, gastroesophageal reflux disease; IQR, interquartile range; NA, not applicable; PIPO, pediatric intestinal pseudo-obstruction; SBS, small bowel scintigraphy; TPN, total parenteral nutrition.

between the solid and liquid SBS in non-PIPO patients. There is a significant difference in age (median age of 15.79 vs 7.76 years), but why this would affect the results is not known. Moreover, when patients diagnosed with lower GIMD were excluded, the colonic filling at 6 hours in non-PIPO patients studied with solid and liquid test meals was quite similar, with a median colonic filling percentage of 65% and 73%, respectively. Therefore, a colonic filling of >65% at 6 hours could be used as a potential cutoff value for normal SBS with both solid and liquid test feeds.

This study found a significant negative correlation between solid SBT and the ADM GLASS score. This means a more severe abnormality on ADM is associated with a more prolonged SBT, if the SBS was performed with solids. It is worth noting that liquid GES may not be as specific as solid GES (22). However, a previous study showed that liquid GES correlated well with solid GES, and an additional assessment of liquid GES could help identify patients with delayed gastric emptying particularly those with normal solid GES (23). In our cohort, most patients underwent liquid GES because patients with suspected PIPO commonly had history of solid or even liquid food intolerance. Hence, the study is limited because of the lack of solid GES. In addition, a lack of correlation between

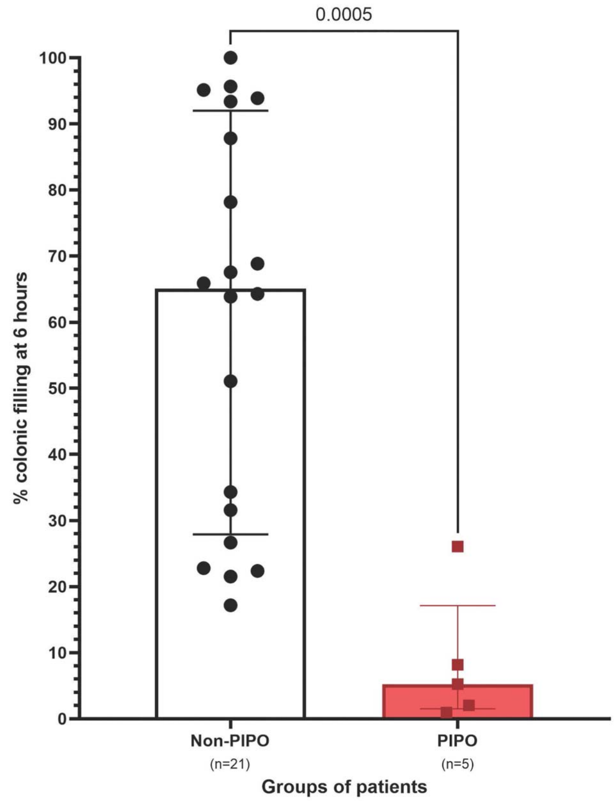

Figure 4. The percentage of colonic filling at 6 hours after solid meal ingestion in 21 non-PIPO and 5 PIPO patients. PIPO, pediatric intestinal pseudo-obstruction.

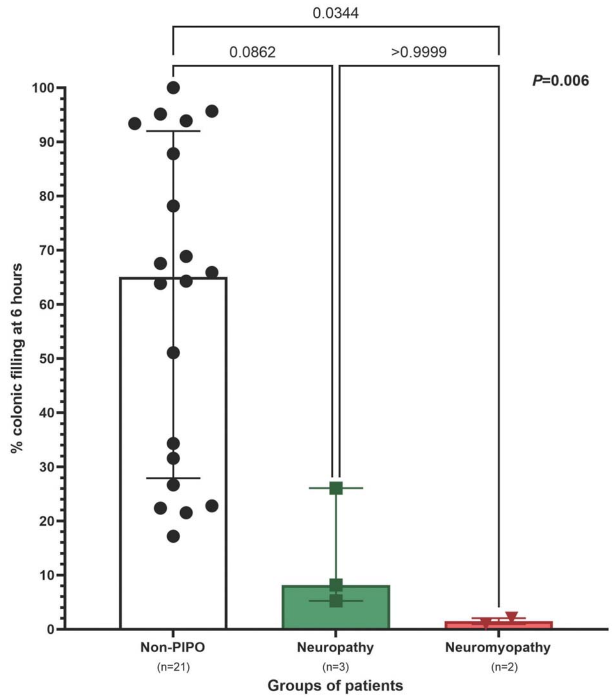

Figure 5. The colonic filling at 6 hours after solid meal ingestion in non-PIPO and PIPO patients classified subtype by enhanced antroduodenal manometry analysis. PIPO, pediatric intestinal pseudo-obstruction.

liquid SBT and ADM parameters could be explained by the methods used to determine the amount of bolus transfer, and the variability of transit times in patients with neuropathic PIPO, particularly rapid SBT in some neuropathic patients (21,24). Only a small number of patients had both SBS performed with liquid and solid meals and ADM. Hence, it was challenging to draw any conclusions on the association between each pair of the tests. In addition, liquid SBS may not be able to fully distinguish patients with neuropathic PIPO from non-PIPO patients because there is a considerable overlap of these 2 groups.

In summary, solid SBS provided better diagnostic accuracy for the diagnosis of PIPO, with higher sensitivity, specificity, and negative predictive values, as compared to liquid SBS. However, the method may be limited by patient feed tolerance. Although not very sensitive, liquid SBS could identify patients with abnormal small intestinal transit, particularly in those who could not undergo or complete the protocol for ADM monitoring. Thus, we proposed the use of SBS as a screening tool before referring patients for special investigation and treatment in the tertiary centers (Supplementary Figure 2, Supplementary Digital Content 2, http://links.lww.com/AJG/C981).

This study shows promise for the potential utility of SBS as an aid to the diagnosis and characterization of PIPO. The percentage of colonic filling at 6 hours of $<$55% for liquid and $\leq$26% for solid SBS could be used as a potential cutoff value for delayed SBT. Patients with neuromyopathy had extremely slow small intestinal transit. Studies in a larger pediatric population and across different age groups are required. We propose that until the test is better validated in larger studies across centers, SBS may have utility as a screening tool before referring patients for special investigation and treatment in the tertiary centers.

CONFLICTS OF INTEREST

Guarantor of the article: Nikhil Thapar, MD, PhD.

Specific author contributions: A.C.: preparation of synopsis data, analysis and interpretation of data, drafting the article, critical revision of the manuscript, and approval of the final version of the paper. E.M.: preparation of synopsis data, critical revision of the manuscript, and approval of the final version of the paper. L.B.: analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper. M.E.: analysis and interpretation of data and approval of the final version of the paper. B.G.: analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper. K.J.L.: recruitment of the patients, analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper. A.R.: recruitment of the patients, analysis and interpretation of data, and approval of the final version of the paper. S.E.: analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper. N.T.: conception and study design, analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper. O.B.: recruitment of the patients, analysis and interpretation of data, critical revision of the manuscript, and approval of the final version of the paper.

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Study Highlights

WHAT IS KNOWN

- ✓ Small bowel scintigraphy (SBS) has potential utility to objectively measure small bowel transit in adults.
- ✓ In adults, normal small bowel transit is defined if ≥40% of radiotracer has reached the colon at 6 hours.
- ✓ SBS has not been validated in children.

WHAT IS NEW HERE

- ✓ SBS provides a well-tolerated and practically feasible assessment of small intestinal motility in children.
- ✓ The test can be performed by extending data acquisition from gastric emptying studies.
- ✓ SBS shows a potential utility as an aid to diagnose and characterize pediatric intestinal pseudo-obstruction, particularly in pediatric intestinal pseudo-obstruction patients with myopathic involvement.

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