A single-center audit of the indications and clinical impact of prolonged ambulatory small intestinal manometry

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Abstract

Background: Small bowel manometry is a diagnostic test available only in a few specialized referral centers. Its exact place in the management of refractory symptoms is controversial.

Methods: The records of all patients who underwent 24-hour ambulatory duodeno-jejunal manometry over a 6-year period were retrospectively reviewed. We studied the clinical indications for small bowel manometry, and reviewed the impact of manometric findings on the clinical outcome. One hundred and forty-six studies were performed in 137 patients (46M, 91F) with a mean age of 44.9 ± 15.7 years. Mean follow-up duration was 15.1 ± 22.6 months. Appropriate endoscopic, radiological and gastric scintigraphy studies were performed in all patients prior to small bowel manometry. Criteria for abnormal motor activity were based on Bharucha's classification.

Key Results: The indications for small bowel manometry were chronic abdominal pain ($n = 43$), slow-transit constipation ($n = 17$), refractory gastroparesis ($n = 16$), chronic diarrhea ($n = 7$), recurrent episodes of subocclusion ($n = 16$), postsurgical evaluation ($n = 36$), suspicion of gut involvement in systemic disease ($n = 9$), and unexplained nausea ($n = 2$). The most common finding was a normal 24-hour ambulatory small bowel manometry ($n = 113$). Thirty-three studies yielded abnormal findings which included extrinsic neuropathy ($n = 6$), intrinsic neuropathy ($n = 18$), intestinal myopathy ($n = 2$), and subocclusion ($n = 7$). Ambulatory small bowel manometry excluded a generalized motility disorder in 77% and had a significant impact on the subsequent clinical course in 23%.

Conclusions & Inferences: Ambulatory small bowel manometry is a useful and safe diagnostic tool to complement traditional investigative modalities in patients with severe unexplained abdominal symptoms.

KEYWORDS

myopathy, neuropathy, small bowel motility, small intestinal manometry

1 | INTRODUCTION

The technique of small bowel manometry is a diagnostic modality, which is only available in a few specialized referral centers. Through intraluminal measurement techniques, insight is obtained

in gastrointestinal (GI) physiology and pathophysiology motility disorders.¹ In the fasting state, the motility of the stomach and small intestine is characterized by a cyclic pattern of contractions, the migrating motor complex (MMC).² The first detailed description of the MMC by Szurszewski et al.² in 1969 of intestinal MMCs in dogs

paved the way for numerous studies of the physiological and pathophysiological significance of the MMC. His findings on the MMC pattern were confirmed in man in 1977 by Vantrappen et al.³ who also reported that absence of MMC was an important risk factor for bacterial overgrowth in humans, establishing an important role for the MMC as intestinal housekeeper and regulator of interdigestive flow.⁴

Small bowel motility can be recorded by manometry⁵ and by various transit tests.^{6–8} While stationary manometry with the use of external transducers and water perfused tubes was frequently applied in the past,^{9–13} the establishment¹⁴ and implementation of ambulatory techniques^{15–18} have allowed continuous ambulatory readings during day and night. Due to prolonged recordings with solid-state systems, response to meals and diurnal variation in motor activity can be assessed, allowing more adequate evaluation of interdigestive motility abnormalities.¹⁹ In addition, nocturnal recordings are helpful in defining phase 3 activity of the MMC²⁰ and provide important data used to form a more accurate diagnosis.^{21–23} Although specific diseases cannot be diagnosed by small bowel manometry alone, it allows for an assessment of the functional integrity of the bowel.^{20,24,25}

Evaluation of patients thought to have a small bowel motility disorder has been performed with either stationary small bowel manometry (range of 6–8 hours)^{26–32} or prolonged ambulatory recording (range of 16–72 hours) in a number of studies to date.^{18,20,23,31,33–44} However, since the last report⁴⁴ in 2009, large-scale studies on the clinical utility of prolonged ambulatory monitoring are lacking.

The aim of this study was to evaluate the role of ambulatory small bowel manometry in clinical management. For this purpose, we conducted a retrospective analysis of the indications, manometric findings and clinical impact of all 24-hour ambulatory small bowel manometry studies performed at the University Hospitals Leuven, Belgium over a 6-year period. A reappraisal of this diagnostic modality is timely today, more than 30 years since the first reported study.⁴⁵ In line with technological advances in catheter design, transducer device and recording software, prolonged ambulatory small intestinal manometry is now performed with increasing ease. To our knowledge, our study represents the largest series of patients undergoing 24-hour ambulatory small bowel manometry at a tertiary referral center reported to date.

2 | MATERIALS AND METHODS

2.1 | Subjects

We performed a retrospective review of all small bowel manometry studies performed by the Department of Gastroenterology at the University Hospitals Leuven, Belgium over a 6-year period. Case records were reviewed and data extracted for patient demographics, clinical history, investigations performed and outcome after small bowel manometry. We evaluated 137 consecutive patients (46 males, 91 females, mean age 44.9 ± 15.7 years, age

range 14–79). The patients were referred to our center for further evaluation of symptoms suggestive of intestinal dysmotility. In addition to routine clinical examination and appropriate blood chemistry, the diagnostic evaluation generally included endoscopy, abdominal imaging as computed-tomography/ultrasound, small bowel radiology, breath tests for bacterial overgrowth and gastric emptying studies where appropriate. Mechanical bowel obstruction and other organic or anatomical lesions were excluded prior to small bowel manometry evaluation. Informed consent was obtained from all patients prior to small bowel manometry, and the Ethics Committee of the hospital previously approved the study.

2.2 | Recording technique

Recordings of duodenal and jejunal intraluminal pressures were performed using a 250-cm-long silicone catheter (OD 4 mm) with 6 solid-state pressure transducers (Konigsberg Instruments, Pasadena, CA, USA) mounted on it. A second single-lumen catheter with a latex bag at its end that could be filled with air was attached to the silicone catheter to accelerate the passage of the probe until correct positioning was achieved. Calibration of the pressure sensors was performed in a pneumatic chamber at room temperature. The probe was introduced orally and positioned under fluoroscopic control in such a way that the proximal first group of 3 sensors, which were 4 cm apart, was located in the descending part of the duodenum. The other group of 3 sensors, which were also 4 cm apart, was located in the jejunum with the first sensor of this group being 30 cm distal to the last sensor of the first group of 3 sensors. After correct positioning, the latex bag was deflated and the probe connected to a portable digital recording device (Digitrapper, Synectics, Sweden). The Digitrapper had an internal memory of four megabytes. The sampling frequency used was 4 Hz for each of the 6 recording channels, which is suitable for accurate reproduction of analog motility signals.¹⁵ Endoscopic guided insertion of the manometry catheter was utilized in cases where pyloric intubation through the pylorus was unsuccessful.

2.3 | Study design

At least 72 hours before the study, patients were instructed to stop any medication known to affect GI motility. Patients were admitted to hospital for the purpose of the 24-hour small bowel manometry study. Following an overnight fast of at least 12 hours, the recording probe was introduced as described above and secured to the subject's nose with adhesive tape. The subjects were asked to ingest 2 standardized meals of equal caloric load (800 kcal; meatloaf, mashed potatoes and apple sauce) and chemical composition (40% fat, 45% carbohydrates, 15% protein). One meal was administered around 12 noon, the second meal between 5 and 6 PM. Subjects were not allowed to eat or drink anything else but water during the study. They were fully ambulant during the study, but were asked to refrain from smoking or vigorous exercise. Subjects were provided a diary

FIGURE 1 Age distribution of patients in the study

to record meal times, as well as the times during upright and supine position.

2.4 | Analysis of motility parameters

At the end of the 24-hour study, the data stored in the Digitrappet were downloaded to a personal computer for visual display and analysis. Recordings of duodenojejunal motor activity were analyzed visually. Results were compared with studies in healthy controls done in our center previously.⁴² Pressure changes <5 mm Hg and identifiable artifacts were excluded from analysis. Criteria for abnormal motor activity were based on the classification proposed by Bharucha et al³⁰ and data collected previously from our center.⁴² Patterns of activity were classified as follows:

1. Normal pattern: normal MMC activity in small bowel with normal fed response.
2. Intestinal myopathy: characterized by decreased amplitude of contractile activity but preserved normal organization of motor activity.
3. Extrinsic (autonomic) neuropathy: characterized by lack of response to a meal and failure to establish a fed pattern of motility.
4. Intrinsic (enteric) neuropathy: characterized by contractile activity of normal amplitude but abnormal configuration and migration pattern of phase III of the MMC, including retrograde propagation, simultaneous occurrence and/or absence of a phase III over a 24-hour period.
5. Patterns suggestive of intestinal obstruction, such as prolonged clustered contractions in the postprandial period or long bursts of phasic activity.

Bursts were defined as periods of ≥ 2 -minute duration with continuous high amplitude (≥ 20 mm Hg) and high frequency (10-12/min) phasic pressure activity that were not propagated and not followed by motor quiescence. Clusters of clinical significance were defined as an uninterrupted sequence of at least 3 rhythmic contractions that was not a component of a phase III of the MMC and was separate from the next motor event by a quiescent period of at least 5 seconds duration, and which was identified in at least 2 jejunal sensors, and lasting for a threshold of at least 20 minutes.²² The subsequent analysis was done with a computer program previously developed and validated in our unit and described in detail elsewhere.⁴⁶

We considered the clinical impact of ambulatory small bowel manometry as clinically relevant when one of the following conditions was fulfilled:

1. Confirmation of a clinical suspicion of a motility disorder, resulting either in a definitive diagnosis or the need for a diagnostic surgical procedure.
2. Exclusion of a generalized motility disorder as part of preoperative evaluation in patients considered for surgery.
3. Determination of extent of motility disorder in the presence of a systemic disease, such as diabetes mellitus.
4. Influence on the decision to start total parenteral nutrition (TPN). This is based on a single study suggesting that the outcome of motility studies might determine need for TPN.²⁴

In addition, we analyzed the charts for other motility tests (mainly gastric emptying tests and ¹⁴CO₂-glycylcholate breath test for bacterial overgrowth.^{47,48}

3 | RESULTS

3.1 | Patient information

One hundred and thirty-seven patients (46M, 91F) with a mean age of 44.9 ± 15.7 years (range 14-79) underwent 146 studies. The patient age and sex distribution are illustrated in Figure 1. Eight patients underwent a repeat study. Mean recording time was 21.3 ± 3.2 hours (10.6 ± 6.3 hours during the day and 10.7 ± 5.8 hours during the nighttime). Five (3.6%) patients required endoscopy in order to advance the catheter through the pylorus. All except 1 patient tolerated the entire duration of the study.

3.2 | Indications for manometry

The predominant indications for performing small bowel manometry are summarized in Table 1. The most common indications were unexplained chronic abdominal pain in 43 patients (29.5%) and post-surgical evaluation in 36 patients (24.7%) with symptoms suggestive of dysmotility. The postoperative studies were performed in patients who had undergone either partial ($n = 11$) or total ($n = 12$) gastrectomy, previous small bowel resection ($n = 5$), previous Nissen

TABLE 1 Summary of the indications for ambulatory small intestinal manometry

Indications	No (%)
Chronic abdominal pain	43 (29.5)
Slow-transit constipation	17 (11.6)
Refractory gastroparesis	16 (11)
Chronic diarrhea	7 (4.8)
Subocclusion	16 (11)
Unexplained abdominal symptoms after surgery	36 (24.7)
Evaluate for presence of gastrointestinal involvement in systemic disease	9 (6.2)
Unexplained nausea	2 (1.4)

fundoplication (n = 2), and 6 patients who had undergone bariatric surgery.

3.3 | Findings on small intestinal manometry

The most common finding was a normal 24-hour ambulatory small bowel manometry, as reported in 113 studies (77.4%), illustrated in Table 2 together with the abnormal findings classified by the clinical indications for the study. In the patients, with unexplained nausea and chronic constipation, in this series, the small bowel manometry did not have an impact on the treatment choice. Thirty-three (22.4%) studies yielded abnormal findings which included findings suggestive of extrinsic neuropathy (6 studies), of intrinsic neuropathy (18 studies), of intestinal myopathy (2 studies) and of mechanical subocclusion (7 studies).

3.4 | Clinical impact

Table 3 summarizes the clinical impact for performing manometry classified by clinical indication.

TABLE 2 Summary of manometry findings obtained from 24-hour ambulatory small intestinal manometry, according to the Bharucha's classification.³⁰

	Normal	Myopathy pattern	Extrinsic neuropathy	Intrinsic neuropathy	Clustering
Chronic abdominal pain	40			2 (prolonged simultaneous contractions)	1
Slow-transit constipation	14			1 (prolonged simultaneous contractions)	2
Refractory gastroparesis	13			2 (hypomotility)	1
Chronic diarrhea	5			1 (bursts and absence of phases 3), 1 (intestinal hypermotility with high amplitude phases 3)	
Subocclusion	8		1	2 (absent phase 3), 1 (bursts with abnormally propagated phase 3), 3 (severe intestinal hypomotility)	1
Unexplained abdominal symptoms after surgery	24	2	4	3 (Retrograde phases 3), 1 (severe hypomotility)	2
Evaluate for presence of gastrointestinal involvement in systemic disease	7		1	1 (absent phase 3)	
Unexplained nausea	2				
Total	113	2	6	18	7

3.4.1 | Confirmation of a clinical suspicion of a motility disorder, resulting in either a definitive diagnosis or the need for a diagnostic surgical procedure

The most significant impact of small bowel manometry lies in its ability to document motility abnormalities that are not detected by other non-invasive radiological imaging or nuclear scintigraphy techniques. This is especially important in unraveling motor disorders that result in functional obstruction. One example are patients with a previous Roux-en-Y gastroenterostomy, developing the so-called Roux syndrome with retrograde propagation of motility in the afferent jejunal limb due to an inversion of the slow wave gradient.^{27,49} Symptoms suggestive of this syndrome include postprandial abdominal pain, bloating, nausea, and vomiting attributed to a functional obstruction within the Roux limb caused by motor asynchrony.²⁷ In the absence of a structural obstruction, small bowel manometry remains the only modality to clearly identify abnormal motility patterns in these subjects.

We confirmed the clinical suspicion of Roux-en-Y syndrome in 3 patients. We were able to identify this syndrome through retrograde phase 3s, consistent with a diagnosis of Roux-en-Y syndrome. Figure 2 illustrates these manometric features in 1 patient.

A decision for diagnostic laparoscopy and full thickness intestinal biopsy was made in 5 patients with recurrent episodes of small intestinal subocclusion and features of intrinsic neuropathy on manometry. Intestinal biopsy confirmed presence of myenteric ganglionitis in 2 of 5 patients who underwent open biopsy.

3.4.2 | Exclusion of a generalized motility disorder as part of preoperative evaluation in patients considered for surgery

Prior to definitive surgery, manometry was performed to exclude a generalized motility disorder in 9 subjects. Following a normal

TABLE 3 Summary of clinical impact of small bowel manometry classified by clinical indication

	Confirm motility disorder	Preoperative evaluation	GI involvement in systemic disease	Influence decision for TPN
Chronic abdominal pain			9	1
Slow-transit constipation		3		
Refractory gastroparesis	1	1		3
Subobstruction	3	1		3
Unexplained abdominal symptoms after surgery	5	4		9
Total	9	9	9	16

FIGURE 2 Illustration of clustered contractions in the small bowel. Manometry sites in the stomach (S1-3) and the duodenum (S1-3). The arrows indicate clustered contractions. The sensors were 4 cm apart

study, a subtotal colectomy for slow-transit constipation (STC) was performed in 3 subjects, surgical correction of superior mesenteric artery syndrome in 1 subject; a venting ileostomy in 1 patient with recurrent episodes of subacute small bowel subocclusion, and conversion of prior Bilroth I to a Bilroth II gastrectomy in 4 subjects.

3.4.3 | Determination of extent of motility disorder in the presence of a systemic disease, such as diabetes mellitus

Seven patients with diabetes mellitus and 2 patients with scleroderma who presented with recurrent symptoms of abdominal pain and vomiting underwent small intestinal manometry to evaluate the extent of GI involvement. We documented failure of the fed response in the postprandial phase in 1 patient with diabetes mellitus, consistent with an extrinsic (autonomic) neuropathy. In contrast, 1 patient with scleroderma showed presence of a normal fed response in the day time but disrupted MMCs and complete absence of nocturnal phase 3s lending support to an enteric (intrinsic) neuropathy.

3.4.4 | Influence decision for TPN

The role of manometry in predicting response to feeding in adults has not been well studied. One previous study has shown that abnormal jejunal motility is an important predictor of intolerance to tube feeding in the postoperative period.²⁴ A total of 16 patients in our series received TPN. Table 4 summarizes the patients' symptoms who received enteral and parenteral feeding. However, a normal or abnormal outcome on small bowel manometry did not directly influence the decision to start TPN or not. In fact, it seemed that this was mainly determined by the general wellbeing and ability to eat by the patient, and the outcome of manometry did not help this decision.

The most common finding was a normal study in 113 studies (77%). These studies were predominantly performed in patients who had recurrent episodes of unexplained abdominal pain, for whom prior extensive investigations either conducted at our hospital or by the referring center were inconclusive. In these patients, a normal small bowel manometry complemented extensive prior diagnostic investigations and provided reassurance for both the patients and the referring physicians. Table 5 shows the manometric findings in patients who received enteral and parenteral feeding.

Subgroup	PEG/PEJ	TPN
Chronic abdominal pain	1	1
Gastroparesis	5	3
Subocclusion	1	3
Unexplained abdominal symptoms after surgery	7	9
Total	14	16

TABLE 4 Summary of patients who received enteral and parenteral feeding

3.5 | Correlation between other investigations

The available diagnostics that were additionally or precedingly performed in this patient series did not correlate with the outcome of the small bowel manometry results. A Spearman correlation coefficient was calculated for the available other motility diagnostics. The gastric emptying of solids ($n = 88$) and liquids ($n = 69$) showed a correlation coefficient of $-.07$ ($P = .52$) and $-.067$ ($P = .59$), respectively, both non-significant. The bile acid breath tests ($n = 61$), which we use to diagnose bacterial overgrowth, correlation coefficient was $.25$ ($P = .054$) and was borderline non-significant.

4 | DISCUSSION

Almost a decade was required for small bowel manometry to pass from the confines of the research laboratory to its role as a clinical diagnostic tool.⁵ In comparison to previous small bowel manometric studies, our study provides the largest number of patients who underwent a 24-hour ambulatory small bowel manometry at a single center to date.

From a clinical perspective, the status of small bowel manometry remains uncertain, although it is being used as a valid diagnostic tool in a number of specialized centers. The ambiguity lies in the invasive nature of the test, the need for dedicated equipment and considerable expertise with limited available therapeutic options. Adequate catheter placement is challenging in patients who may have functional gastric outlet obstruction.²⁸ It is therefore not surprising that it cannot be recommended as a single investigative modality for the diagnosis of functional dyspepsia or irritable bowel syndrome.⁵⁰ In our series, only 5 patients required endoscopic catheter insertion in order to advance the catheter through the pylorus. However, despite the invasiveness of this test, it is generally well-tolerated,

as confirmed in our study, where 99% of patients tolerated the full 24 hours of the study.

Abnormalities of small bowel manometry are non-specific, with considerable overlap between health, disease and in between diseases^{31,40,44,50} as illustrated by the presence of clustered contractions in both diarrhea-predominant IBS and healthy controls^{33,51} or the presence of the MMC in normal transit constipation and STC.⁴⁴ There are also interpatient and inpatient differences in measurements.⁴³ In addition, it is important to note the imperfect correlation between clinical symptoms and physiological measurements for motility disorders.^{40,52,53} This may be due to symptoms caused by abnormalities in segments of the small bowel not studied, such as abnormal tonic contractions in the ileum in patients with IBS.⁵⁴ The discrepancy between subjective symptoms and objective findings contributes to the challenge of treating motility disorders, reinforcing the important role of clinical judgement in the decision making process. To analyze the qualitative values and aid in this decision making process, healthy volunteer studies have been performed by Soffer et al.⁴³ and Scott et al.²¹

To review our experience, we focused on the clinical utility of small bowel manometry, rather than on the actual sensitivity and specificity of various manometric findings in different subgroups of patients with gastrointestinal motility disorders. This approach was also used in studies by Bryne et al.²⁰, Soffer et al.³⁷ and by Lindberg et al.³¹ The confident exclusion of a generalized GI motility disorder in patients, with prior extensive evaluation and negative findings, occurred in 75% of our study population. This is reassuring for patients, whose quality of life may be impaired by the severity of their symptoms and the uncertainties of their diagnosis.²⁴ As described by Lindberg et al., all patients with chronic intestinal pseudo-obstruction (CIPO) had abnormal small bowel motor activity.³¹ For physicians dealing with such difficult cases, a normal finding is convincing, and helps to redirect therapeutic options away from severe intestinal disorders and may help to consider other possibilities, such as underlying psychological disorders^{10,24} or functional bowel disorders, although small bowel manometry is no routine diagnostic test for these diseases.^{31,55} In patients with idiopathic STC, a normal preoperative small bowel manometry is an accurate predictor of long-term outcome after colectomy.⁴¹ In addition, the pharmacological effects of drugs^{56,57} or pathophysiology of disorders⁵⁸ can be investigated.

Yet another crucial role of small bowel manometry lies in its ability to demonstrate a functional obstruction in the absence of a mechanical obstruction on radiological imaging as illustrated by our 3 patients who were diagnosed with Roux-en-Y syndrome. Motility

TABLE 5 Manometric findings in patients who received enteral and parenteral feeding

Manometric findings	PEG/PEJ	TPN
Normal	11	8
Myopathy	0	2
Extrinsic neuropathy	1	1
Intrinsic neuropathy	2	5
Total	14	16

disturbances in the Roux limb have been widely reported previously.^{49,59,60} As shown in our study and similar to previous studies, retrograde propagating waves were consistently present.

Two patients in our series had manometric features of severe hypomotility and low amplitude phasic waves. Following diagnostic laparoscopy and full thickness intestinal biopsy, a diagnosis of myenteric ganglionitis was made, indicating a neuropathic rather than a myopathic underlying abnormality. The manometric findings, pointing in the direction of a myopathy, did not seem to correlate with the pathology findings in the biopsy. Similarly, Lindberg et al. reported that manometric findings could not differentiate between myopathic or neurogenic disorders.³¹ A recent study of Malagelada et al., in which the myopathic manometry pattern did not correlate with signs of enteric myopathy on histopathology, with similar results for neuropathic manometry patterns and their histopathology, confirms this finding.⁶¹ Despite the varied clinical presentation of CIPO and the different manometric findings described in the literature, the usefulness of manometry lies in its ability to demonstrate proof of generalized gastrointestinal (GI) dysmotility in a patient.

We report an important role of ambulatory small bowel manometry in carefully selected patients, based on our experience at a single center over a 6-year period. Our studies were performed, in a tertiary motility center over a long period in time, in a highly selected group of patients, who underwent this investigation only after prior extensive clinical evaluation had been performed. It is not advised performing small bowel manometry in all patients with chronic abdominal pain. It is undeniable that selection bias may well have accounted for the relatively high clinical yield. Acknowledging these limitations of small bowel manometry, we do not recommend the widespread application of small bowel manometry in daily routine clinical practice. Its use should even be restricted to referral centers where experiences can be gained concerning these motility disorders. Rather, our study reinforces the clinical value of this diagnostic tool in carefully selected instances. Patients should only be referred for this test after extensive imaging to rule out obvious mechanical factors, and only in case of debilitating symptoms (eg, inability to maintain adequate oral nutrition intake) or additional indications of a potential major motility disorder (dilated loops on imaging, visible distention or visible peristalsis upon clinical examination, previous surgery like for instance Roux-en-Y). Small intestinal motility disorders remain a relatively under investigated area.⁶² Hence, the continued use of small bowel manometry will provide further insight into the pathogenesis of these complex disorders.

As in other parts of the GI tract, small bowel manometry is now also moving to high-resolution catheter use.⁶³⁻⁶⁵ We anticipate that this may lead to improved understanding of underlying pathophysiological mechanisms, but future analysis will reveal whether it improves diagnostic yield and whether it impacts on therapy choices.

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DISCLOSURE

None of the authors has any competing interests that are relevant to the manuscript.

AUTHOR CONTRIBUTION

JT designed the study; DA acquired the data and analyzed the data; DA and JP drafted the manuscript; TV and JT critically reviewed the manuscript. All authors approved the final version.

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