GI Supply
Specialty Endoscopic Products

LABORIE

The Solar GI™ is an all-in-one customizable system with the widest range of catheters and leading world class software

- Economical & Customizable
- Latest Chicago & London Classifications
- Wide Range of Standard & Customizable Catheters
- Upgradable without Additional Capital Costs

Visit gi-supply.com today to learn more about our product line.

(800) 451-5797 | info@gi-supply.com | gi-supply.com

Disclaimer: GI Supply is an authorized distributor of Laborie Medical Technologies Corp. in the United States of America

Solar GI is a trademark of Laborie Medical Technologies Corp.

Scan here to Learn More

Received: 26 March 2020 | Revised: 10 June 2020 | Accepted: 17 June 2020

DOI: 10.1111/nmo.13937

ORIGINAL ARTICLE

Neurogastroenterology & Motility NGM WILEY

An international survey on clinicians' perspectives on the diagnosis and management of chronic intestinal pseudo-obstruction and enteric dysmotility

Dipesh H. Vasant[1,2] | Loris Pironi[3] | Giovanni Barbara[3] | Federico Bozzetti[4] | Cristina Cuerda[5] | Francisca Joly[6] | Manpreet Mundi[7] | Peter Paine[2,8] | Michael Staun[9] | Kinga Szczepanek[10] | André Van Gossum[11] | Geert Wanten[12] | Simon Lal[2,8]

[1]Manchester University NHS Foundation Trust, Manchester, UK

[2]University of Manchester, Manchester, UK

[3]University of Bologna, Bologna, Italy

[4]University of Milan, Milan, Italy

[5]HGGM Nutrition Unit, Madrid, Spain

[6]MICI et Assistance Nutritive, Clichy, France

[7]Mayo Clinic, Rochester, MN, USA

[8]Salford Royal NHS Foundation Trust, Salford, UK

[9]University of Copenhagen, Copenhagen, Denmark

[10]Stanley Dudrick's Memorial Hospital, Skawina, Poland

[11]Erasme Hospital, Anderlecht, Belgium

[12]Radboud University Medical Center, Nijmegen, The Netherlands

Correspondence
Dipesh H. Vasant, Neurogastroenterology Unit, Manchester University NHS Foundation Trust, Wythenshawe Hospital, Manchester, UK.
Email: dipesh.vasant@mft.nhs.uk

Funding information
No external funding was received for this study.

Abstract

Background: Chronic intestinal pseudo-obstruction (CIPO) and enteric dysmotility (ED) are small intestinal motility disorders defined by radiological and manometric criteria. In the absence of consensus guidelines, we surveyed opinions on the diagnosis and management of CIPO and ED among experts from different countries.

Methods: A survey questionnaire was circulated electronically to members of the European society for Clinical Nutrition and Metabolism, European Society of Neurogastroenterology and Motility, and United European Gastroenterology. Only responses from participants completing all required components were included.

Key Results: Of 154 participants, 93% agreed that CIPO and ED should be classified separately. Overall, 73% reported an increasing incidence of CIPO and ED, with hypermobile Ehlers-Danlos Syndrome the group with the largest increase in referrals (37%), particularly in the UK ($P < .0001$). The majority (95%) find diagnosing CIPO and ED difficult. Notably, antroduodenal manometry, a test mandated to diagnose ED, is infrequently used (only 21% respondents use in >50% cases) and full thickness biopsies were reported to seldom influence medical treatment, nutritional management, and prognosis. Respondents reported that very few treatments are useful for most patients, with bacterial overgrowth treatment, prucalopride, and psychological therapies felt to be the most useful. While only 23% of clinicians felt that parenteral nutrition (PN) improves gastrointestinal symptoms in >50% of cases, 68% reported PN dependency at 5 years in the majority of cases.

Conclusions and Inferences: These data highlight the difficulties with diagnosing and managing CIPO and ED and underscore the urgent need for international, multidisciplinary, clinical practice guidelines.

KEYWORDS
chronic intestinal pseudo-obstruction, enteric dysmotility, gastrointestinal neuromuscular disorders, manometry, parenteral nutrition

1 | INTRODUCTION

Recent international studies have confirmed that small intestinal motility disorders represent a common cause of chronic intestinal failure requiring long-term parenteral feeding, accounting for up to 18% of adult patients requiring long-term parenteral nutrition (PN).[1,2] Moreover, in recent years, it has been suggested that there may be an upward trend in the number of newly diagnosed patients with motility disorders requiring long-term PN.[3,4] Despite this increase, in the absence of universally agreed national or international guidelines criteria, treatment of small intestinal dysmotility may be delayed, contributing adversely to chronicity of symptoms, nutritional status, quality of life, morbidity, mortality, and reported exposure to inappropriate surgeries.[5,6]

Based on findings from radiological and motility tests, small intestinal dysmotility can be sub-classified into chronic intestinal pseudo-obstruction (CIPO) and enteric dysmotility (ED).[6-10] CIPO is defined as chronic/recurrent obstructive type symptoms with radiological features of dilated intestine with air/fluid levels in the absence of any lumen-occluding lesion.[7,9] By contrast, ED refers to patients with objective evidence of small bowel dysmotility on antroduodenal manometry (ADM), but without radiological features of a dilated intestine.[10,11] There is some evidence that outcomes are significantly worse in patients with CIPO compared to ED, with a higher requirement for long-term PN dependency, higher mortality, and complications including small intestinal bacterial overgrowth and the need for surgical interventions.[6,12] However, there remains considerable debate among clinicians on the merits of sub-classifying small intestinal dysmotility into CIPO and ED. The debate predominantly relates to the limitations of ADM as a diagnostic test, due to its invasiveness, which often results in poor tolerance, variability in results, poor correlation with symptoms and histopathology, apparent limited impact on patient management, and lack of availability.[5,7,11,13,14] Another contentious issue in the diagnosis and classification is the role of full thickness biopsies. While patients with small intestinal dysmotility have been shown to have a high incidence of gastrointestinal neuromuscular disorders (GINMD),[12,15] the diagnostic utility and the risk: benefit ratio of performing a full thickness small bowel biopsy remains unclear,[8] despite publication of international consensus guidelines for histopathological diagnosis of GINMD.[16,17]

Therefore, in the absence of well-defined national or international clinical practice guidelines, we hypothesized that there would be a variation in opinions and clinical practice between experts across Europe in diagnosing and managing CIPO and ED.

The aim of this survey was therefore to evaluate current opinions on the diagnosis and management of CIPO and ED among international clinical practitioners.

Key Points

- The majority of expert clinicians believe that chronic intestinal pseudo-obstruction (CIPO) and enteric dysmotility (ED) should be recognized separately.
- Clinicians find making the diagnosis of ED particularly challenging due to current limitations of diagnostic tests for small intestinal dysmotility, often resulting in delayed diagnoses.
- Current best management is multidisciplinary with gut-brain neuromodulators, treatment of bacterial overgrowth, prokinetics, clinical psychology, with careful nutritional assessment and support.

2 | MATERIALS AND METHODS

2.1 | Questionnaire structure

A thirty-nine item questionnaire evaluating clinical practice and opinions on the diagnosis and management of CIPO and ED was developed by the Home Artificial Nutrition & Chronic Intestinal Failure specialist interest group of the European society for Clinical Nutrition and Metabolism (ESPEN), in conjunction with representatives from, the British Society of Gastroenterology Neurogastroenterology and Motility section committee (DV and PP), and the European Neurogastroenterology and Motility (ESNM) society (GB).

An electronic, web-based survey tool (select survey.net, version 4; Class Apps Inc.) was used to generate the survey questionnaire and collect data. The study questionnaire is available in Data S1.

Following detailed discussions and review within the ESPEN specialist interest group, the study questionnaire was structured into the following subsection surveys:

1. respondent's clinical background, sub-speciality, nationality, institution type, and institutional access to multidisciplinary staff and services.
2. incidence of CIPO and ED sub-types in the participant's clinical practice.
3. participant's practice and opinions on various diagnostic approaches to CIPO and ED.
4. participant's approach and opinions on the efficacy of various approaches to the therapeutic management of patients with CIPO and ED.

5. participant's opinions on managing intestinal failure secondary to CIPO and ED, including their experience of long-term PN and caseload in this cohort of patients, their opinions of PN outcomes in CIPO and ED sub-types, and opinions on the role of intestinal transplant.

This study was designed to survey the practices and opinions of clinicians with an interest in CIPO and ED, primarily targeting those in advanced clinical nutrition roles/intestinal failure teams or luminal gastroenterologists with a sub-speciality interest in neurogastroenterology and motility. Participants were provided with definitions of CIPO and ED within the questionnaire, as an aide-memoire for the questions that followed about the two sub-types (Page 3 Data S1).

It was agreed that sections 1-4 (above) would be applicable to all participants. However, it was recognized that section 5 was a specific set of questions only applicable to participants working in a chronic intestinal failure setting with significant experience in long-term PN management and intestinal transplant referrals. Therefore, those without intestinal failure experience were automatically directed to the end of the questionnaire by the online survey software on completion of section 4. Only responses from participants working in centers with >20 patients on long-term PN[18] were included in the analyses for section 5.

Data were collected in the form of single or compound answer multiple-choice questions, drop-down menu questions for numerical data, and there were open ended box questions for descriptive explorations of clinical practice. Prior to launch, the questionnaire was piloted in the UK on national clinical interest groups within clinical nutrition and neurogastroenterology to test usability, understanding, clarity, and question flow.

2.2 | Questionnaire distribution

An invitation to participate with a weblink to the questionnaire created by the survey software was circulated electronically via newsletters published for members of the following international societies; ESPEN, ESNM, and United European Gastroenterology. Clinicians identified by the international study team who have an interest and expertise in GID were also invited to participate in the survey via email. Survey data were collected from March 2018 to October 2018. No patient-related clinical data were collected, so ethical approval was not required for this study.

2.3 | Statistical analysis

Survey data were analyzed using counts and proportions. Comparative analyses were performed using a commercially available software package (Stats Direct v3.1.1, UK).

3 | RESULTS

3.1 | Responder demographics

Overall, 154 participants, (UK 40%, Europe 43%, and Non-European Countries 17%) completed sufficient questions to be included in the study.

Most responders were gastroenterologists (66%), a further 16% were sub-specialists in neurogastroenterology and motility, 12% were gastrointestinal surgeons, and 6% were intestinal transplant clinicians. Overall, 56% had a sub-specialty interest in intestinal failure and 85% were consultants/attending clinicians or clinical academics/ professors.

3.2 | Incidence of CIPO and ED in the participant's clinical practice

The majority of responders (93%) agreed that CIPO and ED should be recognized as separate entities. The majority of responders see ≤10 new referrals with suspected or confirmed CIPO and ED per year (<5 cases: 27%; 6-10 cases: 32%; 11-20 cases: 25%; 21-30 cases: 5%; 31-40 cases: 3%; 41-50 cases: 4%, and >50 cases: 3%).

Of referrals seen with suspected CIPO or ED, 60% of participants reported that only up to a quarter of cases meet clinical and radiological criteria for CIPO (Table 1). Moreover, 65% reported noticing a recent change in the proportion of small intestinal dysmotility referrals with CIPO and ED. More than half (51%) reported observing an increase in the incidence of ED alone, whereas fewer felt there has been an increase in CIPO alone (7%) or both sub-types (15%). In many clinicians' experience, diagnoses of both CIPO and ED are often delayed by 1-5 years (Table 2). Many participants also reported that a

TABLE 1 Clinicians' estimate of the percentage of new referrals with small bowel dysmotility that meet clinical radiological criteria for CIPO (n = 154)

Proportion of referrals meeting CIPO criteria	Number of respondents (%)
0%-25%	92 (60)
25%-50%	37 (24)
50%-75%	17 (11)
75%-100%	8 (5)

TABLE 2 Clinicians' estimate of time between symptom onset to GID diagnosis

Average time to reach diagnosis	CIPO diagnosis n = 154 (%)	ED diagnosis n = 154 (%)
<6 mo	14 (9)	10 (6)
6-12 mo	45 (29)	24 (16)
1-5 y	70 (45)	91 (59)
5-10 y	23 (15)	25 (16)
>10 y	2 (1)	4 (3)

TABLE 3 Changes in the frequency of secondary causes of CIPO/ED

Associated conditions	% reporting increase in related secondary CIPO/ED
Scleroderma	13
Neurological disorders (eg, mitochondrial disorders)	11
Endocrine disorders	9
Ehlers-Danlos syndrome/joint hypermobility disorders	37
Paraneoplastic disorders	7
Autoimmune disorders	4
Autonomic dysfunction (eg, postural orthostatic tachycardia syndrome)	10
Others	3

secondary cause for dysmotility is found in fewer than half of cases. When reviewing a list of secondary causes of CIPO and ED, they reported that the largest increase in referrals has been in patients with Ehlers-Danlos syndrome/joint hypermobility (Table 3), although this trend may be isolated to the United Kingdom (45/61 of participants in UK vs 11/93 of participants in other countries, $x^2 = 61.2$, $P < .0001$).

3.3 | Participant's practice and opinions on diagnostic approaches in suspected CIPO/ED

Most participants agreed that CIPO/ED diagnoses are difficult to make, and only 5% found them straightforward. In particular, the majority of participants (56%) found ED to be a difficult diagnosis, while only 10% reported that CIPO is a more difficult diagnosis. The reasons that participants most frequently selected for difficulties and diagnostic delays in >50% of cases included non-specific symptoms (70%), lack of awareness of CIPO/ED among non-specialists (70%), limitations of diagnostic tests (63%), psychological co-morbidity (58%), and difficulty eliminating opioids as the cause (47%).

Clinicians reported that they request a variety of tests to establish a diagnosis of CIPO or ED. While gastric emptying and x-ray colonic transit tests are the most popular investigations, ADM is rarely performed (Figure 1). Clinicians were also surveyed regarding their practice of requesting full thickness biopsies. Referral patterns for full thickness biopsy did not differ between specialists with an interest in neurogastroenterology and motility (NGM) and the rest of the surveyed respondents (NGM vs other clinicians; never request 2/22 (9%) vs 16/131 (12%), $P > .99$; routinely request 0/22 (0%) vs 5/131 (4%), $P > .99$; only when specimens available from previous or planned surgery 8/22 (36%) vs 42/131 (32%), $P = .81$; and when the diagnosis is unclear 9/22 (41%) vs 57/131 (44%), $P > .99$).

The general consensus among participants was that full thickness biopsies seldom change management and outcomes. Interestingly NGM clinicians, who are often involved in the advanced diagnostic work-up of these patients', trended toward even less positive views on the role of full thickness biopsies than the rest of participants, especially when it came to opinions on their role in determining the prognosis and choice of prokinetic treatment (Table 4).

3.4 | Opinions on the efficacy of various management options for CIPO and ED

While very few options appear to benefit the majority of cases, clinicians reported that the most effective options were neuropathic analgesia, antibiotics for small intestinal bacterial overgrowth,

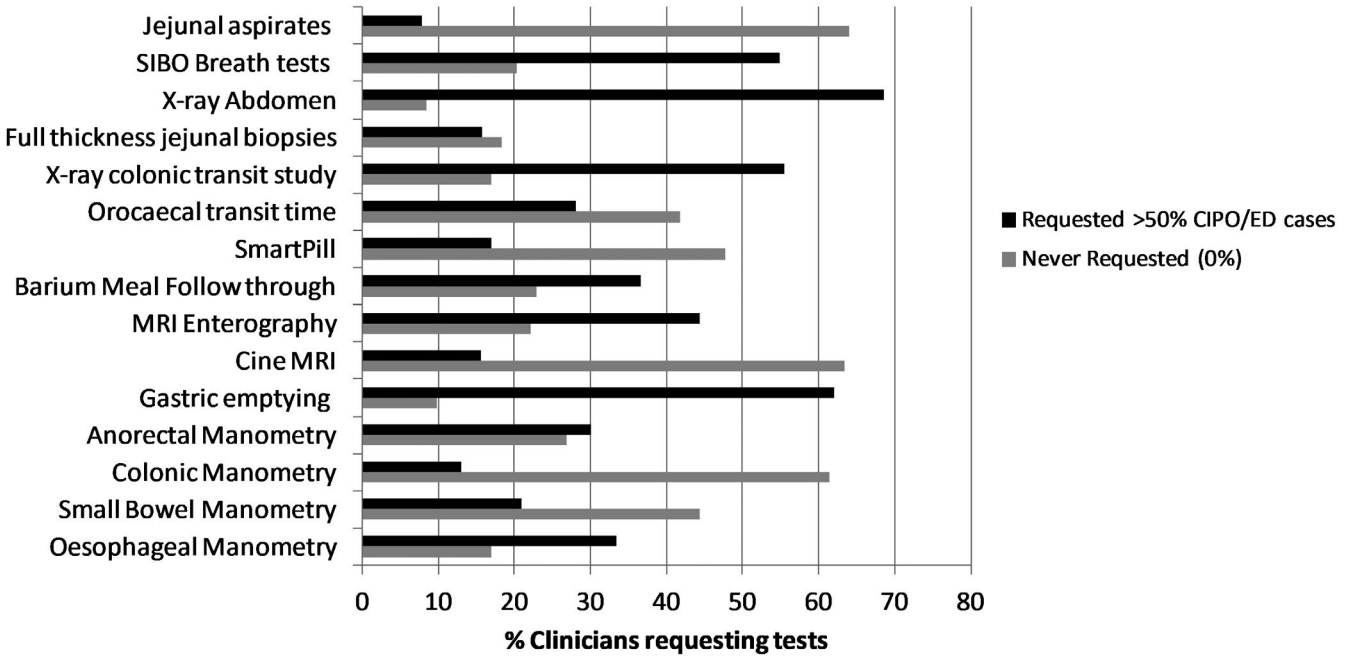

FIGURE 1 Summary of motility investigations requested by participants in suspected CIPO and ED

TABLE 4 Clinicians' opinions on the clinical utility of full thickness biopsies (n = 153 responses; one respondent skipped this question)

Full thickness biopsies	Never	1%-25% cases	25%-50% cases	>50% cases	Not sure
Can lead to targeted medical therapies, for example immunosuppression					
NGM clinicians	23%	59%	14%	5%	0
Other clinicians	11%	40%	17%	13%	19%
Fisher's exact test, *P* values	.15	.11	.75	.28	
Influence nutritional management (oral vs enteral vs parenteral)					
NGM clinicians	36%	41%	18%	5%	0
Other clinicians	21%	33%	18%	18%	11%
Fisher's exact test, *P* values	.12	.47	.91	.12	
Influence surgical decisions					
NGM clinicians	27%	45%	14%	14%	0
Other clinicians	16%	28%	18%	25%	13%
Fisher's exact test, *P* values	.23	.12	.69	.25	
Influence choice of prokinetics					
NGM clinicians	59%	27%	5%	9%	0
Other clinicians	20%	34%	11%	18%	14%
Fisher's exact test, *P* values	.0003	.58	.36	.34	
Help determine prognosis					
NGM clinicians	18%	45%	23%	14%	0
Other clinicians	7%	24%	25%	31%	14%
Fisher's exact test, *P* values	.12	.04	.83	.10	

prucalopride, and clinical psychology (Table 5). Participants reported psychological co-morbidity in patients with CIPO and ED. Patients with ED were reported to exhibit more psychological co-morbidity according to 56% of respondents than those with CIPO. Only 9% felt that patients with CIPO have more prevalent psychological problems, and 35% felt psychological co-morbidity does not differ between CIPO and ED sub-types. Healthcare utilization, including length of hospital stay, was reportedly fairly similar between those with ED and CIPO, for example, 36% participants opined that ED patients have a higher readmission rate than those with CIPO, while 28% believed that patients with CIPO are more likely to be readmitted.

TABLE 5 Clinicians' opinions on the efficacy of treatments for CIPO and ED

	Never (0%)	1%-25% cases	25%-50% cases	>50% cases
Domperidone	15	43	29	13
Metoclopromide	10	45	29	10
Erythromycin	13	44	30	11
Prucalopride	19	31	30	18
Linaclotide	34	34	21	9
Octreotide	38	41	15	5
Neostigmine/ Pyridostigmine	31	44	16	7
Cisapride	66	15	13	5
Naloxegol	43	37	15	5
Antibiotics for SIBO	2	22	41	27
Neuropathic analgesics	10	29	43	15
Opiates	52	35	13	0
Venting gastrostomy	13	55	22	8
Venting colostomy	48	39	8	4
Enteral feeding	9	43	36	10
Parenteral nutrition	5	36	36	19
Psychology	13	29	30	22
Surgery	20	66	12	3

Interestingly, 52% of those surveyed reported that they have referred patients with suspected small bowel motility disorders that do not meet CIPO or ED criteria, for consideration of long-term PN. The reasons for these patients not meeting either CIPO or ED criteria included lack of availability of small bowel motility studies (23%), small bowel motility studies not tolerated (11%), enteral feeding tube not tolerated (37%), and clinical decision not to order small bowel motility tests (7%). Inappropriate surgeries appear to be fairly common in suspected CIPO/ED cases, with a prevalence of 10%-50% of cases according to 66% of respondents.

3.5 | Survey of clinical experience and practice with long-term PN in CIPO and ED related chronic (type 3) Intestinal Failure

A total of 59 participants work in units with ≥20 patients on long-term PN. Patients with CIPO or ED make up none of their HPN caseload according to 2 respondents, 1%-10% of their long-term PN patients according to 19 respondents, 10%-25% of cases according to 32 respondents, 25%-50% according to 5 respondents, and >50% of

TABLE 6 Clinical opinions on the utility of HPN in CIPO and ED related intestinal failure in reducing complications among long-term PN specialists

	Never (0%)	1%-25% cases	25%-50% cases	>50% cases	Skipped question
Dehydration	1 (2)	19 (33)	11 (19)	26 (46)	2
Metabolic impairments	2 (4)	18 (32)	14 (25)	23 (40)	2
Quality-of-life	4 (7)	16 (28)	13 (23)	24 (42)	2
Bacterial translocation	29 (51)	21 (37)	6 (11)	1 (2)	2
Gastrointestinal symptoms	6 (11)	22 (39)	15 (27)	13 (23)	3
Aspiration pneumonia	18 (32)	26 (46)	5 (9)	7 (13)	3
Hospital admissions	5 (9)	22 (39)	14 (25)	16 (28)	2

TABLE 7 Opinions on predictive factors for long-term PN dependency in CIPO/ED

	Never (0%)	1%-25% cases	25%-50% cases	>50% cases	Skipped question
Primary vs secondary CIPO/ED	8 (14)	15 (27)	15 (27)	18 (32)	3
Full thickness biopsy result	12 (21)	17 (30)	10 (18)	17 (30)	3
Tolerance of oral or enteral intake	0 (0)	5 (9)	10 (18)	42 (74)	2
Manometry findings	23 (41)	24 (43)	5 (9)	4 (7)	3
Age at diagnosis	6 (11)	27 (47)	10 (18)	14 (25)	2
Long-term opiate use	0 (0)	12 (21)	12 (21)	33 (58)	2
Psychological factors	0 (0)	7 (12)	17 (29)	34 (58)	1

cases according to 1 respondent. Interestingly, 36 of the 59 clinicians managing long-term PN reported that 1%-10% of their long-term PN population have suspected small bowel dysmotility without meeting CIPO or ED criteria, while a further 13 clinicians reported that as many as 10%-25% of their long-term PN caseload did not meet CIPO or ED criteria but required long-term PN for a suspected small bowel motility disorder. According to most participants, long-term PN often improves hydration and metabolic impairments, but improves gastrointestinal symptoms less often, with only 23% reporting symptom benefit in >50% of cases (Table 6). Moreover, it was the opinion of 68% of clinicians, who were managing long-term PN, that once long-term PN is commenced, >50% of CIPO and ED patients will be dependent on PN at 5 years. Clinicians were also surveyed on factors which they felt are important in predicting the long-term need for PN. Psychological factors, tolerance of enteral feeding, and opioid use were felt to be the most important predictive factors, whereas manometry findings were felt to be the least important factor (Table 7).

There were mixed views on long-term PN complications in patients with CIPO/ED. Participants were asked to compare the incidence of catheter complications between CIPO/ED and other causes of chronic intestinal failure. Only 7% of clinicians felt that catheter complications are less frequent in CIPO/ED than other causes of intestinal failure, whereas 68% felt they are more frequent, and 25% reported that catheter complication rates are similar to other causes of intestinal failure. Intestinal failure-associated liver disease (IFALD) rates were reported to be similar to other causes of intestinal failure by 73% of clinicians. The vast majority of respondents (86%) indicated that ED has a higher psychological co-morbidity than other causes of intestinal failure, while 41% have indicated that patients with CIPO have higher psychological co-morbidity than other indications for long-term PN. Opinions were again divided on long-term PN 5-year survival rates in patients with GID. 24% believed survival outcomes are better for CIPO/ED than Crohn's related intestinal failure, 45% believe they are similar, and 31% believe that outcomes are poorer than for Crohn's disease.

Finally, participants were surveyed on their views on intestinal transplant in CIPO and ED. Forty-nine respondents had experience in making intestinal transplant referrals for patients with chronic intestinal failure. Of these participants with experience, the majority (76%) reported that they would refer patients with both CIPO and ED for transplantation if necessary, 16% would never refer an ED patient, and 14% would not refer patients with either CIPO or ED for transplant assessment.

4 | DISCUSSION

This is the first large-scale survey on the diagnosis and management of CIPO and ED and confirms that there is currently a wide variation in clinical practice internationally. These data also identify that diagnostic delays are reported to be common in CIPO and ED and provide some important insights into the difficulties currently faced by clinicians investigating and managing these patients, which could be addressed in future consensus guidelines. The comprehensive

survey also provides information for the first time on the perceived clinical utility of various motility tests, the clinical efficacy of currently available treatments, and the role of long-term PN and intestinal transplantation.

The survey data strongly support the importance of recognizing CIPO as a separate clinical entity, and this would be consistent with clinical data which have shown that the CIPO sub-type is associated with a significantly worse prognosis.[6,12] The trends in referrals seen by those surveyed suggest that there is an increase in referrals with the ED sub-type, with CIPO often making up less than 25% of referrals. While there were no major changes reported in the referral rates of primary and secondary CIPO/ED, there was a notable reported increase in referrals with CIPO and ED secondary to hypermobile Ehlers-Danlos syndrome. However, when compared to respondents from other countries, the majority of clinicians who noted this trend were from the UK. The associations between functional gastrointestinal disorders and hypermobile Ehlers-Danlos are increasingly recognized,[19] and recent data from a UK population have shown a very high prevalence of functional gastrointestinal disorders in patients with hypermobile Ehlers-Danlos syndrome, with 84% meeting the diagnostic criteria for functional disorders in multiple gut regions.[20] The reasons for this trend being specific to UK participants are unclear, but may stem from an awareness being higher due to most of the studies to date emanating from the UK. It would seem unlikely that increased awareness alone, however, would drive an increase in severe clinical presentations requiring nutrition support. Further international collaborative epidemiological research on the prevalence of hypermobile Ehlers-Danlos syndrome related dysmotility would therefore be required to investigate this further.

Interestingly, the survey data show that clinicians are more confident in making a diagnosis of CIPO compared to ED. The exact reasons for this difference remain unclear, but the ease of interpretation and availability of radiological investigations to achieve a CIPO diagnosis are a clear advantage when compared to using ADM to diagnose ED. ADM is not widely available, is difficult to interpret, often poorly tolerated, and in this, survey was surprisingly rarely used in establishing diagnoses. The survey data show that clinicians are, instead, using a variety of segmental motility and imaging modalities to characterize the pattern of dysmotility and are using pragmatic approaches including intolerance of small bowel feeding in many cases, even when referring patients with suspected functional and motility disorders for parenteral feeding.

The survey data therefore highlight the need for better diagnostic tests for ED. There are a number of promising techniques including wireless motility capsule[21,22] and Cine MRI[23-25] which are being evaluated and are available in some centers, but were only routinely available for 16%-17% of respondents in this survey. However, in the interim, as proposed by Paine et al, a more pragmatic approach to diagnosing severe gastrointestinal dysmotility can be adopted.[8] This approach would not mandate ADM for an ED diagnosis. Instead, this pragmatic approach takes into consideration those with suggestive symptoms, abnormal motility in >1 region on segmental investigations, or abnormal GI neuromuscular histopathology (when available), with evidence of small bowel involvement, either abnormal ADM, abnormal small bowel transit test, or intolerance of small bowel feeding.[8]

Diagnostic delays appear to be fairly common in CIPO and ED.[12,26] The survey data suggest a lack of awareness of this group of disorders among non-specialists. This is clearly important as diagnostic delays and lack of knowledge may explain the high incidence of inappropriate surgical interventions that have not only been identified in this survey, but also in several clinical studies.[12,14,27] Delayed diagnosis may also significantly impact the patients' psychological well-being [28] and have been shown in other functional gastrointestinal disorders to be associated with stigmatization.[29] Therefore, there is a clear need to raise awareness of CIPO and ED with appropriate educational strategies among the wider clinical community including gastroenterologists and associated specialists such as surgeons and dieticians in order to prevent diagnostic delays, potentially hazardous surgical interventions, and improve clinical outcomes.

In addition to difficulty with diagnosis, respondents also further highlighted the lack of efficacy of many of the established therapies for CIPO and ED. Strategies which ranked best included treatment of bacterial overgrowth, clinical psychology, the pan-enteric prokinetic prucalopride, PN, and neuropathic analgesia. When considering the latter, it is noteworthy that patients with ED in particular often exhibit severe neuropathic/centrally mediated abdominal pain, which responds very poorly to opioids. Indeed opioids can be detrimental in this setting due to their antimotility effects, worsen pain due opioid induced hyperalgesia,[30] and potentially increase infection risk,[31] which is particularly important when considering HPN.[32] The current survey data are thus in accordance with an increasing body of evidence[33] and recently published clinical guidelines to support use of centrally acting gut-brain neuromodulators rather than the standard use of opioid medications to target this type of neuropathic pain.[34,35] Notably, respondents highlighted the importance of the multidisciplinary care including clinical psychology. Since no single treatment was reported to be highly efficacious, it is vital that care is holistic and that the psychological impact of a dysmotility diagnosis is not neglected.[28]

Unfortunately, due to the nature of this study, there was a need to consider maximizing response rates among potential participants. It was therefore important to limit the complexity of the questionnaire and the amount time that would be required for participant completion. Within these constraints, respondents were asked for their impressions, estimates and opinions on the prevalence, incidence and management, rather than provide actual figures from their clinical practice. Another limitation of the study is that participants were not asked to report separately on the efficacy of all the specific treatments between sub-types. It is therefore not possible to determine whether there were any perceived differences in the efficacy of the various medical and non-medical treatment options listed between the CIPO and ED sub-types.

When considering intestinal failure in CIPO and ED, PN was reported to have a role in treating dehydration, metabolic impairment,

and some effect on quality of life in many patients. However, PN was felt to be less effective in managing gastrointestinal symptoms and reducing hospitalization. Once established, survey respondents felt that subsequent long-term PN dependency is fairly high, with some notable factors including; tolerance of oral/enteral feeding, psychological factors, and opioid use reported as being important in predicting the ability to wean PN. Overall, long-term PN was felt to be safe, with the majority of those surveyed reporting either similar or better survival outcomes compared to other causes of intestinal failure. The experiences of the survey participants are consistent with published survival outcomes from long-term PN centers.[3,12,36,37] These data therefore suggest that long-term PN should only be reserved for use as an important life sustaining treatment for patients with CIPO and ED related intestinal failure, and not used to treat symptoms alone.

In summary, this survey has provided valuable clinical experience from a large number of international experts in small bowel dysmotility. The data have demonstrated that in the absence of clear clinical guidelines, diagnosis and management of CIPO and ED is challenging, with a wide variation in practice. The data suggest clinical management of these conditions should be multidisciplinary including gastroenterology/motility, clinical nutrition, pain management, and clinical psychology. We conclude that there is an urgent need for evidence-based, clinical guidelines, to raise awareness of CIPO and ED, reduce diagnostic delays, and improve patient outcomes.

ACKNOWLEDGMENTS

The authors would like to acknowledge the partner societies which supported this study including ESPEN, United European Gastroenterology, ESNM, and the neurogastroenterology and motility section of the BSG. The authors would also like to acknowledge the following participants: Tim Vanuytsel (Belgium), Greger Lindberg (Sweden), Amol Sharma (USA), Christian Hvas (Denmark), Asbjorn Mohr Drewes (Denmark), Magnus Simren (Sweden), Carolina Malagelada (Spain), Mark Fox (Switzerland), Vincenzo Stanghellini (Italy), Jutta Keller (Germany), Per M. Hellstrom (Sweden), Gabrio Bassotti (Italy), Maura Corsetti (UK), Hans Tornblom (Sweden), Lisa Sharkey (UK), Mani Naghibi (UK), Jeremy Nightingale (UK), Konstantine Shemerovskii (Russia), Natalia Zarate-Lopez (UK), Charlotte Pither (UK), Dan M Livovsky (Israel), Fermin Estremera-Arevalo (Spain), Sofia Silva Mendes (Portugal), Yan Yiannakou (UK), Pauline Riviere (France), Sadek Mostafa (Egypt), Usama Hantour (Egypt),Timothy Ambrose (UK), Ashley Bond (UK), Clare Donnellan (UK), Jens F. Dahlerup (Denmark), Giles Major (UK), Peter J Whorwell (UK), Duncan Massey (UK), David Sawbridge (UK), Antje Teubner (UK), Philip Smith (UK), Ramya Kalaiselvan (UK), Peter Mooney (UK), Martyn Dibb (UK), Gemma Wiltshaw (UK), Charlotte Rutter (UK), Klaus Krogh (Denmark), David Armstrong (Canada), Luis Miguel Becerra Granados (Guatemala), Nick Thompson (UK), Jonathan Tyrrell-Price (UK), Michael Glynn (UK), Khalid Sager (UK), Mattias Soop (Sweden), Maria Ines Pinto Sanchez (Canada), Alison Culkin (UK), Stephane M. Schneider (France), Gerard Rafferty (Northern Ireland), Sheldon Cooper (UK), Suzanne C Donnelly (UK), Mia Small (UK), Shaheen Hamdy (UK), Larry Loo (UK), Anna Zmarzay (Poland), Carmen Arraiza (Spain), Anna Demagistris (Italy), Elisabeth De Waele (Belgium), Ingrid Gisbertz (Netherlands), Aurora E Serralde-Ziga (Mexico), Carmelo Loinaz Segurola (Spain), Fernanda Luisa Ceragioli Oliveira (Brazil), Vicente Jose Salles De Abreu (Brazil), Leah Gramlich (Canada), Jose Manuel Moreno Villares (Spain), Kalina Grivcheva Stardelova (Macedonia), Mireille Serlie (Netherlands), Gallitelli Livia (Italy), Paula Ravasco (Portugal), Edda Cava (Italy), Arenas Marquez Humberto (Spain), Gilberto Fabian Hurtado-Torres (Mexico), Donnabelle Navarrete (Philippines), Silcia de Barrio (Argentina), Dechelotte (France), Anders Thorell (Sweden), Leuenberger Michele (Switzerland), Chambrier Cecile (France), Jarosaw Szefel (Poland), Michele Barone (Italy), Adriana Crivelli (Argentina), Fatema Mubarak (Bahrain), Hanna-Liis Lepp (Estonia), H. ne Braet (Belgium), Eduardo Eiras Moreira da Rocha (Brazil), Shestopalov AE (Russia), Inmaculada Moraga Guerrero (Spain), Rinoy Chandran (India), Vaidotas Urbonas (Lithuania), Pascal Probst (Germany), Daniel Lightowler (Australia), Arun Abraham (UK), Asma Fikree (UK), Louise Langmead (UK), Ruth Mckee (UK), Klaartje Kok (UK), Charles Knowles (UK), Taina Sipponen (Finland), Sampsa Pikkarainen (Finland), Colin Ainley (UK), Philip Woodland (UK), Penny Neild (UK), Catherine Fraser (UK), Farooq Rahman (UK), Thomas Bazin (France), Marianna Arvanitakis (Belgium), Yeng Ang (UK), Wadiamu Gashau (UK), Emily Tucker (UK), Maria Luisa Eliana Luisi (Italy), Georgiana- Emmanuela Gilca-Blanariu (Romania), Oana Timofte (Romania), Christopher Calvert (UK), Phil Bliss (UK), Rosa Burgos (Spain), Stephanie Hansel (USA), A N De Silva (UK), Giselle Lopes (Brazil), and Irma Poveda Merlo (Columbia).

CONFLICT OF INTEREST

The authors have no competing interests.

AUTHOR CONTRIBUTIONS

DHV created the questionnaire, analyzed data, and wrote the manuscript; LP contributed to study design, questionnaire distribution/data collection, and helped write the manuscript; GB helped disseminate the questionnaire and with data collection; FB, CC, and FJ helped with study design; MM helped write the manuscript; PP helped with questionnaire design, data collection, and write the manuscript; MS, KS, AVG, and GW all helped with study design and reviewed the manuscript; SL conceptualized the study, and helped with questionnaire design and write the manuscript.

ORCID

Dipesh H. Vasant https://orcid.org/0000-0002-2329-0616
Giovanni Barbara https://orcid.org/0000-0001-9745-0726

REFERENCES

1. Pironi L, Arends J, Bozzetti F, et al. ESPEN guidelines on chronic intestinal failure in adults. *Clin Nutr.* 2016;35:247-307.
2. Pironi L, Joly F, Forbes A, et al. Long-term follow-up of patients on home parenteral nutrition in Europe: implications for intestinal transplantation. *Gut*. 2011;60:17-25.
3. Dibb M, Soop M, Teubner A, et al. Survival and nutritional dependence on home parenteral nutrition: three decades of experience from a single referral centre. *Clin Nutr.* 2017;36:570-576.

4. Smith T, Hirst A, Jones B, Baxter J. *Annual BANS report*. Redditch, Worcestershire: British Association of Parenteral and Enteral Nutrition; 2011.
5. Di Nardo G, Di Lorenzo C, Lauro A, et al. Chronic intestinal pseudo-obstruction in children and adults: diagnosis and therapeutic options. *Neurogastroenterol Motil*. 2017;29(1):e12945.
6. Lindberg G, Iwarzon M, Tornblom H. Clinical features and long-term survival in chronic intestinal pseudo-obstruction and enteric dysmotility. *Scand J Gastroenterol*. 2009;44:692-699.
7. Stanghellini V, Cogliandro RF, De Giorgio R, et al. Natural history of intestinal failure induced by chronic idiopathic intestinal pseudo-obstruction. *Transplant Proc*. 2010;42:15-18.
8. Paine P, McLaughlin J, Lal S. Review article: the assessment and management of chronic severe gastrointestinal dysmotility in adults. *Aliment Pharmacol Ther*. 2013;38:1209-1229.
9. Camilleri M. Intestinal dysmotility: does the X-ray resolve the real dilemma? *J Pediatr Gastroenterol Nutr*. 1997;24:100-101.
10. Wingate D, Hongo M, Kellow J, Lindberg G, Smout A. Disorders of gastrointestinal motility: towards a new classification. *J Gastroenterol Hepatol*. 2002;17(Suppl):S1-S14.
11. Quigley EM. Enteric dysmotility: validating the Wingate/Bangkok classification. *Gastroenterology*. 2010;139:346-348.
12. Vasant DH, Kalaiselvan R, Ablett J, et al. The chronic intestinal pseudo-obstruction subtype has prognostic significance in patients with severe gastrointestinal dysmotility related intestinal failure. *Clin Nutr*. 2018;37:1967-1975.
13. Malagelada C, Karunaratne TB, Accarino A, et al. Comparison between small bowel manometric patterns and full-thickness biopsy histopathology in severe intestinal dysmotility. *Neurogastroenterol Motil*. 2018;30(3):e13219.
14. Billiauws L, Corcos O, Joly F. Dysmotility disorders: a nutritional approach. *Curr Opin Clin Nutr Metab Care*. 2014;17:483-488.
15. Lindberg G, Tornblom H, Iwarzon M, Nyberg B, Martin JE, Veress B. Full-thickness biopsy findings in chronic intestinal pseudo-obstruction and enteric dysmotility. *Gut*. 2009;58:1084-1090.
16. Knowles CH, Veress B, Tornblom H, et al. Safety and diagnostic yield of laparoscopically assisted full-thickness bowel biospy. *Neurogastroenterol Motil*. 2008;20:774-779.
17. Knowles CH, De Giorgio R, Kapur RP, et al. The London Classification of gastrointestinal neuromuscular pathology: report on behalf of the Gastro 2009 International Working Group. *Gut*. 2010;59:882-887.
18. Nightingale JM, Young A, Hawthorne B, et al. *British Intestinal Failure Alliance (BIFA) position statement 2016 on home parenteral nutrition*, Redditch, Worcestershire, UK. 2016.
19. Beckers AB, Keszthelyi D, Fikree A, et al. Gastrointestinal disorders in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type: a review for the gastroenterologist. *Neurogastroenterol Motil*. 2017;29(8):e13013.
20. Lam CY, Palsson OS, Whitehead WE, et al. Rome IV functional gastrointestinal disorders and health impairment in subjects with hypermobility spectrum disorders or hypermobile Ehlers-Danlos syndrome. *Clin Gastroenterol Hepatol*. 2020.S1542-3565(20):30204–4. https://doi.org/10.1016/j.cgh.2020.02.034
21. Farmer AD, Wegeberg AL, Brock B, et al. Regional gastrointestinal contractility parameters using the wireless motility capsule: inter-observer reproducibility and influence of age, gender and study country. *Aliment Pharmacol Ther*. 2018;47:391-400.
22. Rao SS, Mysore K, Attaluri A, Valestin J. Diagnostic utility of wireless motility capsule in gastrointestinal dysmotility. *J Clin Gastroenterol*. 2011;45:684-690.
23. Menys A, Butt S, Emmanuel A, et al. Comparative quantitative assessment of global small bowel motility using magnetic resonance imaging in chronic intestinal pseudo-obstruction and healthy controls. *Neurogastroenterol Motil*. 2016;28:376-383.
24. Fuyuki A, Ohkubo H, Higurashi T, et al. Clinical importance of cine-MRI assessment of small bowel motility in patients with chronic intestinal pseudo-obstruction: a retrospective study of 33 patients. *J Gastroenterol*. 2017;52:577-584.
25. Ohkubo H, Kessoku T, Fuyuki A, et al. Assessment of small bowel motility in patients with chronic intestinal pseudo-obstruction using cine-MRI. *Am J Gastroenterol*. 2013;108:1130-1139.
26. Stanghellini V, Cogliandro RF, De Giorgio R, Barbara G, Salvioli B, Corinaldesi R. Chronic intestinal pseudo-obstruction: manifestations, natural history and management. *Neurogastroenterol Motil*. 2007;19:440-452.
27. Sabbagh C, Amiot A, Maggiori L, Corcos O, Joly F, Panis Y. Non-transplantation surgical approach for chronic intestinal pseudo-obstruction: analysis of 63 adult consecutive cases. *Neurogastroenterol Motil*. 2013;25:e680-e686.
28. Twist K, Ablett J, Wearden A, et al. Gastrointestinal dysmotility: a qualitative exploration of the journey from symptom onset to diagnosis. *Neurogastroenterol Motil*. 2018;30(8):e13339.
29. Hearn M, Whorwell PJ, Vasant DH. Stigma and irritable bowel syndrome: a taboo subject? *Lancet Gastroenterol Hepatol*. 2020;5(6):607-615.
30. Paine P. Centrally mediated abdominal pain syndromes. *Medicine*. 2019;47:354-357.
31. Vallejo R, de Leon-Casasola O, Benyamin R. Opioid therapy and immunosuppression: a review. *Am J Ther*. 2004;11:354-365.
32. Richards DM, Scott NA, Shaffer JL, Irving M. Opiate and sedative dependence predicts a poor outcome for patients receiving home parenteral nutrition. *JPEN J Parenter Enteral Nutr*. 1997;21:336-338.
33. Kilgallon E, Vasant DH, Green D, et al. Chronic continuous abdominal pain: evaluation of diagnostic features, iatrogenesis and drug treatments in a cohort of 103 patients. *Aliment Pharmacol Ther*. 2019;49:1282-1292.
34. Sobin HW, Heinrich TW, Drossman DA. Central neuromodulators for treating functional GI disorders: a primer. *Am J Gastroenterol*. 2017;112:693-702.
35. Drossman DA, Tack J, Ford AC, Szigethy E, Törnblom H, Van Oudenhove L. Neuromodulators for functional gastrointestinal disorders (disorders of gut– brain interaction): a Rome Foundation working team report. *Gastroenterology*. 2018;154(4):1140-1171.e1.
36. Amiot A, Joly F, Alves A, Panis Y, Bouhnik Y, Messing B. Long-term outcome of chronic intestinal pseudo-obstruction adult patients requiring home parenteral nutrition. *Am J Gastroenterol*. 2009;104:1262-1270.
37. Salazar E, Clermont-Dejean NM, Schwenger KJ, et al. Patients with severe gastrointestinal dysmotility disorders on home parenteral nutrition have similar survival as those with short bowel syndrome: a prospective cohort study. *J Parenter Enteral Nutr*. 2020.https://doi.org/10.1002/jpen.1866

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: VasantDH, Pironi L, Barbara G, et al. An international survey on clinicians' perspectives on the diagnosis and management of chronic intestinal pseudo-obstruction and enteric dysmotility. *Neurogastroenterology & Motility*. 2020;32:e13937. https://doi.org/10.1111/nmo.13937