Utility of Colon Manometry in Guiding Therapy and Predicting Need for Surgery in Children With Defecation Disorders

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ABSTRACT

Objectives: Colon manometry (CM) has emerged as a tool to evaluate children with defecation problems. Our aim was to evaluate the utility of CM in guiding therapy and predicting surgery in pediatric constipation.

Methods: Retrospective review of children undergoing CM for 4 indications: constipation, fecal incontinence, postsurgical evaluation and chronic intestinal pseudo-obstruction. Variables included age, sex, follow-up, and CM parameters: gastrocolonic response (GC) and quality/quantity of high-amplitude propagating contractions (HAPCs). Interventions: medical, surgical or no intervention. Outcomes: response to change of therapy guided by CM, response to first intervention guided by CM (CMI) and CM predicting surgery (CMS). Response to therapy was classified according to study indication.

Results: Five hundred fifty-five studies (448 patients, 54.4% female; median age 8.9 years) were included, 24% of studies were normal. Change of therapy guided by CM was associated with a high response rate ($P = 0.003$). Overall response to stimulant laxatives was 48% and was not associated with CM findings. Surgical interventions had a higher response rate than medical or other interventions ($P < 0.001$). We found no association between the CM interpretation and CMI, but an abnormal CM was predictive of surgery ($P < 0.01$). GC and presence/number of HAPCs were not associated with CMI or CMS. We also found no association between HAPC quality and CMI but partially propagated HAPCs were predictive of surgery ($P < 0.001$). Logistic regression analysis showed no factors associated with CMI; however, longer follow up and partially propagated HAPCs were predictive of surgery.

Conclusions: CM is useful in pediatric defecation disorders, although not predictive of successful medical intervention, an abnormal CM is predictive of surgery. CM should be performed only after medical interventions have failed and surgery is contemplated.

Key Words: colon manometry, refractory constipation, treatment outcomes

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What Is Known

- Colon manometry is a useful test in the evaluation of children with constipation.
- Evidence about its utility in guiding therapy and predicting outcomes is limited.

What Is New

- Colon manometry does not predict successful medical interventions, but an abnormal colon manometry predicts need for surgery in pediatric refractory constipation.
- Change of therapy guided by colon manometry is associated with high therapeutic response rate.
- Colon manometry is helpful in guiding therapy in children with refractory constipation and should be performed after all medical interventions have failed.

Constipation is amongst the most common complaints in pediatrics with a prevalence ranging of up to 29% worldwide (1), resulting in an increase in hospital costs and admission rates in the last 2 decades and associated to a significantly negative impact on quality of life for both patients and families (2).

On most occasions, dietary changes, stool softeners and behavioral interventions are sufficient but when treatment fails, it is important to perform evaluations of colonic and anorectal function to understand the pathophysiology of the constipation.

Colon manometry (CM) has emerged over the last 2 decades as an important tool to evaluate colonic function. The guidelines ''Evaluation and Treatment of Functional Constipation in Children'' by the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) suggest that the CM be completed to rule out a colonic neuromuscular disease (3), but is vague on how far medications should be exhausted before the test. CM has been reported to be useful in predicting response to antegrade continence enemas (ACE) (4,5), however, little if any information is known on its utility in guiding initial therapy and predicting long-term outcomes. This study is the largest series of children undergoing CM to date, and the first one to evaluate the utility of the test in guiding therapy and predicting need for surgical interventions.

METHODS

We conducted a retrospective study of patients undergoing CM at our center for evaluation of defecation disorders (constipation and/

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or fecal incontinence), postsurgical evaluation (ACE and ostomy) and chronic intestinal pseudo-obstruction (CIPO) between January of 2006 and December of 2013. IRB approval was obtained. CM was performed as previously described (6). All patients underwent a bowel cleanout with a PEG solution except those with an ileostomy, those with an appendicostomy/cecostomy received high dose oral PEG and ACE irrigations twice per day 24-h before the procedure. The catheter was placed via colonoscopy and under general anesthesia, and the CM was performed the next day. Studies were performed using the MMS equipment and software (Medical Measurement Systems NH). An abdominal film was obtained to verify location of the catheter before starting the study. Meal was not standardized for content or amount and bisacodyl dose was 0.25 mg/kg up to 20 mg. Data collected from medical records included: CM indication, treatment and patient progress, follow-up (months between the CM and last contact with our institution). Therapeutic interventions were classified as medical (changes in medication/dose increases), surgical (colonic resection, ACE, closure/performance of ostomy), or no intervention.

Colon Manometry

The variables in the CM included: gastrocolonic response to a meal or GC (visual increase in colonic activity) and presence, number and propagation of high amplitude propagating contractions or high-amplitude propagating contractions (HAPCs; peristaltic contractions with amplitude ≥60 mmHg and propagating for ≥30 cm). HAPCs were classified as fully propagated when reached the rectosigmoid junction and partially propagated when they did not. CM was defined as normal when there was presence of both GC and fully propagated HAPCs (as defined in the position statement from ANMS and NASPGHAN) (7). CM was performed twice in some patients; analysis was per study not per patient.

Clinical Decision After Colon Manometry

The decision to change therapy after the CM was based on a previously published algorithm (8) (and literature available) in 4 study indications: constipation, chronic intestinal pseudo-obstruction or CIPO, postsurgery evaluation, and organic fecal incontinence; also taking into account the patient's age, symptom duration, medication failure, and disability. Clinical decision process is shown on Figure 1.

Outcome Classifications After Long-term Follow-up

Outcome was evaluated in 3 categories:

1. CM guiding initial therapy (CMI): response to first therapy initiated after CM results.
   a. Response was classified according to the study indications:
   b. Functional constipation (Rome III criteria applied retrospectively): response was defined as ≥3 bowel movements per week, failure as 2 or less bowel movements per week
   c. CIPO: response was defined as improved abdominal distention and enteral tolerance (with medications or ileostomy), failure as persistent symptoms
   d. Postsurgical evaluation (ostomy closure and post-ACE): response was ≥3 bowel movements per week and failure 2 or less bowel movements per week
   e. Organic fecal incontinence (included only those with colorectal malformations): response was defined as <3 incontinence episodes per week and failure ≥3 incontinence episodes per week
2. CM predicting need of surgical therapy (CMS): surgical intervention (antegrade colonic enemas, colonic resection or ileostomy) at the end of follow-up.
3. Association between changing the therapy (or not changing therapy) based on the results of the CM and both CMI and CMS.

Statistical Analysis

SPSS version 23 was used. Continuous variables are expressed as medians (range). Proportions were compared using

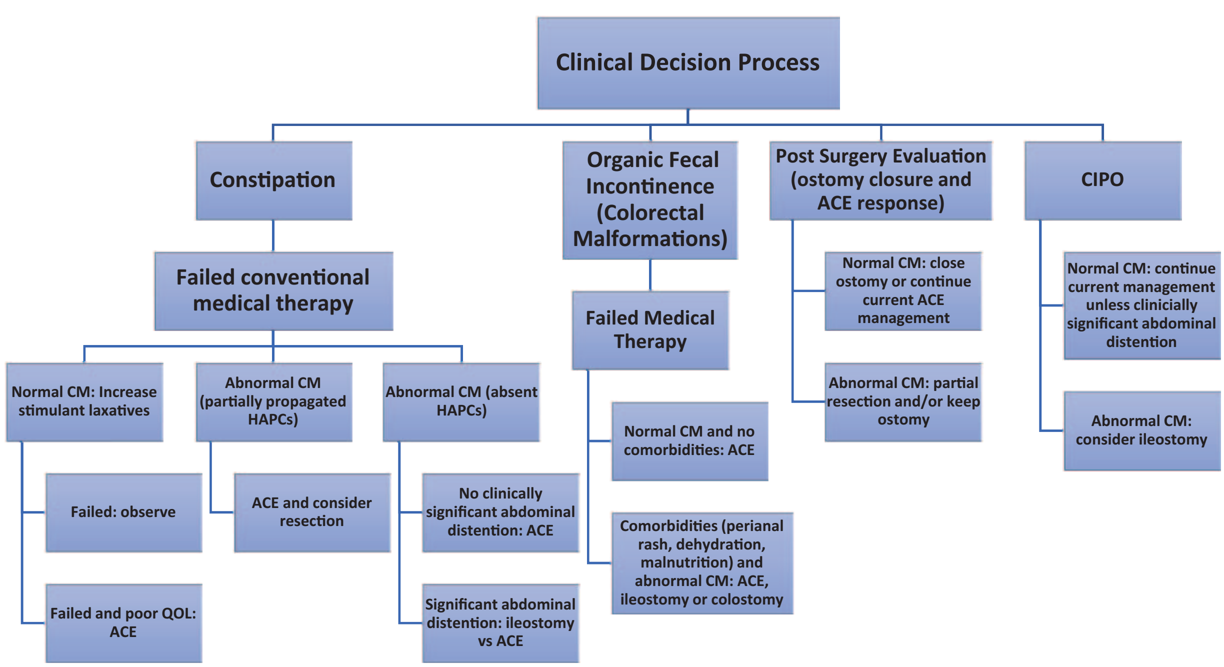

FIGURE 1. Clinical decision process.

χ^2 or Fischer exact tests. Comparisons of continuous variables were done using nonparametric tests (Wilcoxon signed ranks test). Multivariate logistic regression models were used to determine the factors associated with response.

RESULTS

A total of 646 CM studies were performed and follow-up information was available in 555 (86%) and those were included in this study. Median age was 8.9 years (0.8–24 years), 302 (54.4%) were girls and median follow-up was 23 months (1–102 months). A total of 67 (12%) patients underwent repeat studies. The study indications included constipation in 378 (68%), CIPO evaluation in 60 (11%), organic fecal incontinence in 18 (3%) and postoperative indications that included evaluate feasibility of ostomy closure in 53 (10%) and post-ACE evaluation in 46 (8%). Primary diagnosis was idiopathic in 388 (69.9%), colorectal malformations in 64 (11.5%), internal anal sphincter achalasia in 22 (4%), metabolic disorders in 15 (2.7%), short bowel syndrome in 13 (2.3%), spinal anomalies in 12 (2.2%), neuromuscular disorders in 4 (0.7%), and other in 37 (6.7%).

Colonic Manometry

The study was completed in all, however, in 12/555 patients with CIPO did not have meal challenge (severe feeding intolerance) and were excluded from analyses including the GC. The proximal port of the CM catheter was located in the right colon in 485/555 (87.4%), in the transverse colon in 67/555 (8.3%), and in the splenic flexure/descending colon in 24 patients (4.3%). The median number of HAPCs was 4 (0–34). A total of 146/555 (26%) had no HAPCs and 409/555 (73.7%) had HAPCs present. HAPCs propagated from cecum and reach up to the hepatic flexure in 2/409 (0.5%), to transverse colon in 26/409 (6.4%), splenic flexure in 55/409 (13.4%), descending colon in 137/409 (33.5%), sigmoid colon in 109/409 (26.6%) and to rectum in 80/409 (19.6%). CM was normal in 134/555 (24.1%) and abnormal in 421/555 (75.9%).

Recommendations Based on Colonic Manometry

A new medical recommendation was given in 366/555 (66%) patients, including medications (stimulant laxatives in 253, secretagogues in 32, tegaserod in 15, enemas in 1, and other medications in 22), other interventions (pain management in 20) or adjustments to current medications (decrease of ACE irrigations in 23) with an overall successful response in 190/366 (52%). Overall, stimulant laxatives were used in 307 patients, response rate was 48% and was not predicted by CM (80% had an abnormal CM). Surgical intervention was recommended as first intervention in 100 (18%) patients, 84% had an abnormal CM, these interventions included ACE in 43, partial or total colectomy in 15, diverting ileostomy in 21 or colostomy/ileostomy closure in 17, and stricture correction in 4. A total of 79 (79%) of those 100 patients responded to initial surgical intervention. At end of follow-up, a total of 179 (32.3%) patients required surgery. After CM no changes were recommended in 16% and 63% of those were responders.

Association Between Change of Therapy Based on Colonic Manometry Results and Treatment Outcome

A total of 325 patients (58.6%) were considered responders and 230 (41.4%) nonresponders.

We evaluated the potential effect of changing therapy on both CMI and CMS. We found no association between change of therapy and CMI (58% responders among those with change of therapy vs 63% responders with no change in therapy, $P = 0.362$) (see Table 1). We observed a strong association between change of therapy and eventual need of surgery, virtually all patients that required surgery had an initial change of therapy compared with those in whom no surgery was required (99% vs 76%, respectively, $P = < 0.01$).

We also evaluated the effect of changing therapy on the overall response at the end of follow-up and we observed a higher response to therapy in those in whom a change of therapy was recommended compared with those in whom no change in therapy was advised (79% vs 64%, respectively, $P = 0.003$), suggesting the test guides a successful change of therapy (see Table 1).

Factors Associated With a Change of Therapy

We observed that we were more likely to recommend a change of therapy in those with abnormal CM compared with those with normal CM (87% vs 73%, respectively, $P < 0.001$). We also observed that most (75/89 or 84%) in whom we recommended no change in therapy were either CIPO (36 patients), evaluate for ostomy closure (32 patients) and post-ACE evaluation (7); no change in therapy was recommended in only 12 patients with constipation and 2 with fecal incontinence.

We then looked at the CM parameters that guide those decisions and we found no association between change of therapy and GC and presence of HAPCs ($P = 0.41$ and 0.221, respectively) but we observed an association with quality of HAPCs (change of therapy in absent or partially propagated- vs fully propagated HAPCs was 85% vs 69%, respectively, $P < 0.001$). In other words,

TABLE 1. Association between decision of changing therapy and outcome and colon manometry parameters

	Change therapy, n (%)		No therapy change, n (%)		
Outcome	Responders	Nonresponders	Responders	Nonresponders	*P* value
CMI	268/464 (58)	196/464 (42)	57/91 (63)	34/91 (37)	0.388
CM parameters	Normal	Abnormal	Normal	Abnormal	
CM interpretation	96/464 (21)	368/464 (79)	38/91 (42)	53/91 (58)	<0.001
GC* response	371/459 (81)	88/459 (19)	62/84 (74)	22/84 (26)	0.141
HAPCs	96/464 (21)	368/464 (79)	38/91 (42)	53/91 (58)	<0.001

*Number is smaller because of patients that did not tolerate meal during study.
CM = colon manometry; CMI = response to first intervention after colon manometry (outcome to treatment guided by colon manometry results); CMS = need for surgery predicted by CM results; GC = gastrocolonic response; HAPCs = high amplitude propagating contractions.

TABLE 2. Association between colon manometry parameters and need for surgery

	Surgical intervention, n (%)		
CM parameter	Required surgery	Did not require surgery	*P* value
CM normal	26/179 (15)	108/376 (29)	<0.001
Abnormal	153/179 (85)	268/376 (71)	
GC* normal	132/176 (75)	301/367 (82)	0.057
Abnormal	44/176 (25)	66/367 (18)	
HAPC present	124/179 (69)	285/376 (76)	0.103
Absent	55/179 (31)	91/376 (24)	
HAPC fully propagated	26/179 (15)	108/376 (29)	<0.001
Partially propagated	153/179 (85)	268/376 (71)	

Note abnormal HAPC is associated with need for surgery but not absence of HAPC (although there is a tendency towards an association). CM = colon manometry overall interpretation; GC = gastrocolonic response to a meal; HAPC = high amplitude propagating contraction.
*Number is different because of patients that did not tolerate meal during study.

our decision to change therapy was based on the quality of the HAPCs. Including only those with constipation (excluding CIPO and post-ACE response), we observed that we were more likely to change therapy in those with HAPCs present ($P = 0.002$) and not propagating beyond the splenic flexure ($P = 0.023$), in other words, those with partially propagated HAPCs. Excluding those with follow-up <12 months does not change results.

Association Between Specific Colonic Manometry Parameters and Outcome

Overall colonic manometry interpretation

We found no association between the overall interpretation of the CM and CMI (CM was normal in 24% of both responders and nonresponders, $P = 0.92$) but an abnormal CM study is associated with a higher rate of subsequent need for surgery (36% of those with abnormal CM underwent surgery compared with 19% of those with normal CM, $P < 0.01$) (see Table 2).

Gastrocolonic response to a meal

We found no association between gastrocolonic (GC) response and CMI (GC was normal in 79% of responders vs 81% in nonresponders, $P = 0.70$) and we observed a tendency towards an association with CMS (surgery was required in 30% of those with normal GC and in 40% of those with abnormal GC, $P = 0.057$) (see Table 2).

Quality of high-amplitude propagating contractions

We found no association between CMI and both presence of HAPCs (HAPCs present in 72% of responders vs 76% in non-responders, $p = 0.451$) and presence of fully propagated HAPCs (24% in both responders and non-responders, $p = 0.888$). We also found no association between the presence of HAPCs and CMS (surgery was required in 30% of those with present HAPCs and in 38% of those with no HAPCs, $p = 0.103$), however, we did observe an association between absent and partially propagated HAPCs and CMS (HAPCs were abnormal in 85% of those requiring surgery and in 71% of those not requiring surgery, $p < 0.001$). Excluding those with CIPO and post-surgical assessment the results do not change except for presence of HAPC, those with absent HAPCs are more likely to require surgery as well ($p = 0.04$) (see Table 2).

Migration of high-amplitude propagating contractions

We found no association between migration of HAPCs and CMI, however, we did observe an association between HAPC migration and CMS (see Table 3).

TABLE 3. Association between outcome and high amplitude propagating contraction migration

	Outcome, n (%)			
HAPC migration†	CMI	*P* value*	CMS	*P* value*
Splenic flexure				
Responders	218/325 (67)		115/179 (64)	
Nonresponders	164/230 (71)	0.290	267/376 (71)	0.108
Descending colon				
Responders	184/325 (57)		96/179 (54)	
Nonresponders	143/230 (62)	0.190	231/376 (61)	0.081
Sigmoid colon				
Responders	110/325 (34)		46/179 (27)	
Nonresponders	80/230 (35)	0.819	144/376 (38)	0.003
Rectum				
Responders	43/325 (13)		15/179 (8.4)	
Nonresponders	37/230 (16)	0.345	65/376 (17)	0.005

Note the decrease in the rate of responders with increasing migration of HAPCs towards the rectum (normal HAPCs). CMI = colon manometry guiding first therapy; CMS = colon manometry predicting need for surgery
*Compared with nonresponders.
†HAPC migration to most distal colonic segment recorded.

Number of high-amplitude propagating contractions

We found that the median number of HAPCs is not associated with CMI and CMS ($P = 0.980$ and 0.145, respectively). Excluding those with follow up <12 months does not change results.

Association Between Study Indication and Outcome

We evaluated the utility of the CM predicting the need for surgery in each study indication groups as described under methods. For the constipation group (n = 378), we found that surgery was eventually performed in 15% of those with a normal CM versus 39% of those with an abnormal CM ($P = 0.001$). We also observed that surgery was performed in a significantly lower proportion in those with normal GC (31% in normal vs 47% in abnormal, $P = 0.009$) and normal HAPCs (15% in those with normal HAPCs vs 39% on those with abnormal HAPCs, $P < 0.001$) and a tendency towards an association for presence of HAPCS (31% of those with HAPCs present vs 41% of those without HAPCs, $P = 0.065$). Those with a preoperative indication for the CM (n = 99) demonstrated an association between surgery and absence of HAPCs ($P = 0.007$) and a tendency towards an association with abnormal CM, abnormal GC and abnormal HAPCs ($P = 0.078$, 0.08, and 0.078, respectively). The CIPO group was composed of 60 patients, and it showed that an abnormal CM as well as absent and abnormal HAPCs were associated with surgery ($P = 0.017$, 0.001, and 0.017, respectively) but GC was not ($P = 0.128$). In the fecal incontinence group (n = 18), none of the parameters of the CM were associated with need for surgery.

Association Between Type of Intervention and Outcomes

We observed a lower response to initial medical therapy compared with other interventions –surgical and no intervention – (51% vs 67%, respectively, $P < 0.001$). Response to laxative use was lower than all other interventions (48% vs 68%, respectively, $P < 0.001$). We observed a higher response to initial surgical recommendation compared with all other recommendations (79% vs 52%, respectively, $P < 0.001$). We also found that surgery as initial recommendation was associated with higher response compared with medical intervention (79% vs 51%, $P < 0.001$). We also found a higher response rate amongst all those ultimately undergoing surgery (88% vs 271%, $P < 0.001$). Of the 134 with normal CM, a total of 91 had idiopathic constipation and the remainder 43 had CIPO or postsurgery evaluation. A total of 8 of those 91 ultimately required surgery (ACE) and all responded.

Analysis of Joint Effect of Factors Associated With Outcomes

We evaluated the joint effect of factors potentially associated with CMI and CMS, including age, sex, length of follow-up, etiology (idiopathic), GC, and quality of HAPCs. We found no factors associated with CMI, however, we found longer follow-up and absent and/or partially propagated HAPCs to be associated with CMS (Table 4).

DISCUSSION

This is the first article systematically evaluating the utility of the CM in guiding initial therapy and predicting need for surgery, and the largest reporting the utility of CM in children. We observed that even though our medical management was successful in more than half of the patients, the CM is not useful to predict successful outcomes to medical interventions, it is only helpful to predict need and outcome of surgical interventions. These findings are particularly important for the timing and indication of the study, suggesting the CM should be performed when all medical therapies have failed, and surgery is contemplated.

We found that a change of therapy based on the CM is not associated with a successful response to that initial therapy, particularly when this change is medical, but it is associated with a successful overall outcome to any therapy. In other words, changing the course of treatment based on the CM interpretation is associated with an overall successful outcome. The decision to change the therapy after the CM was based not only mainly on the CM results, but also considering the clinical presentation and previous and current medications. One could argue here whether the test is truly useful, given that this data shows that patients respond eventually as therapy options are steadily progressed from medical to surgical until the symptoms are controlled, but the test can help you in that decision process. Our findings demonstrating that a change of therapy is associated with an overall successful outcome support what Pensabene et al. reported previously, that in 95 children followed for a median time of 20 months after the CM, they found that following the recommendation based on the CM results, patients reported symptoms improved in 78%, were unchanged

TABLE 4. Factors associated with successful outcome and need for surgery

	CMI				CMS			
			95% C.I.				95% CI	
	P	Exp. B	Lower	Upper	*P*	Exp. B	Lower	Upper
Age	0.23	0.95	1.01	1.01	0.07	0.97	0.93	1.01
Female	0.17	0.90	1.81	1.81	0.83	1.04	0.71	1.53
Follow-up	0.63	0.99	1.01	1.01	0.00	1.02	1.01	1.03
Organic etiology	0.75	0.64	1.38	1.38	0.52	1.15	0.75	1.75
Abnormal GC*	0.57	0.73	1.76	1.76	0.72	1.09	0.68	1.74
Absent or partially propagated HAPCs†	0.75	0.62	1.41	1.41	0.00	2.16	1.31	3.57

CMI = colon manometry guiding first therapy; CMS = colon manometry predicting need for surgery; GC = gastrocolonic response; HAPC = high amplitude propagating contraction.
*GC: gastrocolonic response to a meal.
†HAPC migration to most distal colonic segment recorded.

in 18% and worse in 4% of patients and 88% of parents stated the recommendations from the CM were helpful (9). In our study, however, we found that despite observing a 52% response rate to medical interventions, the CM was not predictive of such response. One explanation maybe related to our definition of response being more rigorous than theirs. This further support our recommendation of trying all medications before the CM and may also reflect the severity of the constipation.

We observed that an overall abnormal CM does not predict success to initial medical therapy but is associated with eventual need for surgery after medical interventions are exhausted. Some authors have reported the utility of the CM as a predictor of response to surgical interventions, particularly antegrade colonic enemas (ACE) (4,5). Others have also reported colon motility improvement with ACE (4,10), resolution of colon dysmotility being associated with ACE discontinuation (4) and guiding the timing of ostomy closure (11). Singh et al (12) have reported that adults with constipation and normal sigmoid manometry were more likely to respond to medical interventions and biofeedback (and lower rates of surgery) than those with neuropathic changes. No study, however, has evaluated the utility of the total colon manometry in predicting eventual need for surgery and which parameters of the CM can be used as predicting factors. Our data suggests that both an abnormal GC and absent or partially propagated HAPCs are associated with the need for surgery. One explanation is that patients who show colonic dysfunction might be more likely to receive aggressive treatment (surgery), which may account for the better overall outcome. Nevertheless, the data show that this test is designed to identify those with colon dysmotility as the targets of surgical interventions. We also found that the propagation of the HAPCs is important in predicting overall outcome: the less propagation within the colon (more abnormal) the higher the likelihood of eventual need for surgery, supporting again, that those with an abnormal CM are more likely to require surgery.

We found no association between the frequency of HAPCs and both the response to initial therapy and the need for surgery, in other words, having multiple fully propagated HAPCs does not confer any added benefit over having a single fully propagated HAPC.

We also found no association between demographics and CM variables and initial response to therapy (CMI) but we found an association between longer length of follow-up and absent or partially propagated HAPCs and eventual need of surgery (CMS). With respect to follow-up, it is possible that longer follow-up time permits the evaluation of eventual need of surgery.

The analysis per study indication demonstrated the strong predictive value for the CM and the eventual need for surgery both in the constipation and the CIPO groups, to a lesser degree on the preoperative group evaluation and virtually in none of our patients with organic fecal incontinence. An important limitation of this analysis is the small sample size for the fecal incontinence group.

This study has important limitations, being a retrospective study of patients referred for evaluation to a motility center the most relevant resulting in limited data availability. Given that all this information was obtained through chart reviews, only patients who returned to the hospital for follow-up are included, potentially excluding a large number of patients. Additionally, the baseline management at the local level, and the threshold to order the test varied according to the referral base of the institution. In addition, the treatments recommended to patients are not standardized, in other words those receiving medications may have not received the same doses or in the same frequency and duration. Another limitation is that in some patients, we do not have complete information on the characteristics of the bowel movements or the fecal incontinence, a fact that may limit some of our conclusions.

CONCLUSIONS

In summary, although we found a high response rate of medical interventions, the CM is not predictive of such response, but it is a very useful test in predicting response to surgical interventions and the eventual need for surgery. We, therefore, recommend the CM should be performed after exhausting all medical interventions, including daily stimulant laxatives, and before a surgical intervention is being recommended.

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