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ORIGINAL ARTICLE

# High Prevalence of Anorectal Dysfunction in Ambulatory Patients with Chronic Constipation, Regardless of Colon Transit Time

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## Abstract

**Background** Classification of chronic constipation (CC) into its three subtypes of slow transit constipation, defecation disorder and normal transit constipation, may improve its multifaceted management. We assessed the merits of the London classification in patients with CC, who were studied by both wireless motility capsule (WMC) and high-resolution anorectal manometry (HR-ARM), examining their relative utilities in decision-making.s

**Patients and Methods** Retrospective, community-based study of prospectively collected data on patients with CC by Rome IV criteria, who underwent WMC and HR-ARM, Balloon Expulsion Test, and Rectal Sensory Testing. Clinical assessment was made by standard questionnaires. On WMC, standard criteria for colonic transit time (CTT) were used (normal CTT < 59 h). The hierarchical London classification was used for HR-ARM analyses.

**Results** Of 1261 patients with CC, 166 (91 M; ages 22–86) received technically satisfactory WMC and HR-ARM, formed the analyzed study cohort, of whom 84 had normal CTT and 82 had prolonged CTT (> 59 h). Patients with slow CTT were significantly older and had longer duration and more severe disease. Using the London classification criteria for disorders of anorectal function, we noted a high prevalence of anorectal dysfunction, regardless of CTT. Except for lower rate of anal hypertonicity in patients with slow CTT, disorders of recto-anal coordination, and rectal sensation were seen at a comparable rate in patients with CC, regardless of CTT.

**Conclusion** There is a significant overlap of anorectal disorders in patients with slow CTT. There is questionable specificity and utility of WMC and HR-ARM in assessing patients with CC. More work is needed to demonstrate the value of these studies as surrogate markers of the disease and its response to multifaceted therapy.

**Keywords** Constipation · Wireless motility capsule · High-resolution anorectal manometry · Pelvic floor dyssynergia · Defecation disorder · Slow transit constipation

## Introduction

Constipation is defined as unsatisfactory defecation resulting from infrequent and difficult stool passage or both [1]. It includes a spectrum of symptoms, such as hard stools, excessive straining and incomplete evacuation, infrequent bowel movements, bloating, and abdominal pain, all affecting quality of life (QoL) in up to 5% of the population [2]. Recurrent chronic constipation (CC) results from poor colonic regulation of stool movement, together with uncoordinated or obstructed defecation, with or without simultaneous abnormal gastrointestinal sensitivity. In severe cases, fecal impaction, pseudo-obstruction, volvulus, and colonic perforation may occur, causing significant morbidity and mortality [3].

The Rome IV criteria allow categorization of CC into four subtypes: (a) functional constipation (FC), (b) irritable bowel syndrome with constipation (IBS-C), (c) opioid-induced constipation (OIC) and (d) functional defecation disorders (FDDs), such as inadequate defecatory propulsion and dyssynergic defecation [4]. Based on the presence

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or absence of detectable physiological abnormalities upon diagnostic testing, at least three subtypes of CC (which may overlap) have been described: slow transit constipation (STC), defecation disorder (DD) and normal transit constipation (NTC). Better classification into these three subtypes could improve the management of constipation through a multifaceted approach [5].

Practicing clinicians often diagnose and manage CC more pragmatically, based on abdominal pain, stool frequency, consistency (Bristol scale), and ease of evacuation, but frequently CC remains clinically undifferentiated. To further guide management, tests of colon transit, such as the wireless motility capsule (WMC), and tests of evacuation, such as high-resolution anorectal manometry (HR-ARM), the balloon expulsion test (BET), rectal sensory test (RST), and defecography are often used, based on symptom predominance. For patients suspected of evacuation disorder (ED), the BET and defecography are direct measures of the ability to expel rectal contents, whereas HR-ARM provides information primarily on recto-anal coordination and rectal sensation [6].

Recently, an International Anorectal Physiology Working Group (IAPWG) presented a consensus on the measurement of anorectal function, using HR-ARM [7]. This so-called "London classification" provides clinicians with generally accepted parameters of anorectal function, based on which decisions can be made in a hierarchical fashion, highlighting elements of generally accepted significance and mostly aiming at prioritization in decision-making for patients with symptoms of anorectal dysfunction, after exclusion of pertinent structural abnormalities, typically by colonoscopy.

In this retrospective, community-based, cohort study, we aimed to assess the relative merits of the London classification in patients with undifferentiated functional CC, who were studied by both WMC and HR-ARM, examining their relative utilities in diagnosis and their potential role in facilitating clinical decisions at the point of care of patients otherwise lacking a structural explanation for their symptoms by colonoscopy. We hypothesized that the use of these sophisticated tests would differentiate patients in select subgroups that would be managed differently [8].

## Patients and Methods

This is a retrospective, IRB-approved study of prospectively collected data on patients with clinically undifferentiated functional CC by Rome IV criteria, who underwent both WMC and HR-ARM over 10 years (January 2012 to December 2022) to guide clinical management. The study was conducted at the Silicon Valley Neuro-Gastroenterology and Motility Center, a community-based facility with established referrals for over 15 years. To preserve accuracy and the clinical implications of the study findings, individual and independent clinical record and tracing review was performed on all patients. *Inclusion Criteria:* All patients in the cohort presented for the assessment and quantification of infrequent bowels (constipation), disordered rectal evacuation, rectal sensation disorder, or possible adult Hirschsprung's disease, the identification and quantification of impaired anal sphincter function, functional incoordination, and preoperative assessment before planned partial colectomy, rectopexy or rectocele repair, or before possible pelvic floor physical and biofeedback therapy. All patients had no recent (6–12 months) evidence of colonic obstruction by colonoscopy and all gave verbal consent prior to the procedures. *Exclusion Criteria:* Patients were excluded from analysis if there was evidence of deviation from the standard protocol described in the London classification paper or technical inadequacies of any of the individual studies (both WMC and HR-ARM) were found. Special emphasis was given to ensure that the two studies were performed within a time frame of < 3 months after the initiation of the request for studies and within 1 month from each other and to exclude patients who had an intervening intervention, such as pelvic floor physical therapy, biofeedback anal botulinum toxin injection, or anorectal surgery.

Symptom frequency and severity were not assessed using standardized questionnaires typically used in therapeutic pharmacologic trials of STC, but instead, on questionnaires used in our clinical practice for each relevant symptom, such as lower abdominal pain, infrequent evacuation of hard stools, incomplete stool evacuation, and straining at evacuation (absent = 0, mild = 1, moderate = 2, and severe = 3). This questionnaire has been used for more than 20 years in our practice, is easy and practical, and reported in many of our previous studies. The questionnaire is practical for patients to fill upon entry to initial and follow-up visits and it serves as an opportunity for patients and the physician to semi-quantify symptoms prior to a consultation [9–12].

### HR-ARM Technique, BET, and RST

For the conduct of HR-ARM in our laboratory, we have been using a stabilization period of 2–3 min after catheter insertion, followed by measurements of basal (resting) anal tone (in mmHg) over one minute, while the patient remains relaxed (maximal anal sphincter basal pressure) [6]. The subsequent squeeze period records the anal pressure during voluntary effort to contract the anus/pelvic floor. Three squeezes are then performed, each for 5 s, separated by 30 s. The highest value (maximal anal sphincter squeeze pressure) is then counted (in mmHg). An endurance squeeze follows, with a sustained voluntary effort over 30 s, aiming to assess fatigue over time, followed by a recovery period. The rectal sensory test (RST) assesses rectal sensitivity to

balloon distension utilizing a rectal balloon placed proximal to the anal canal, recording the volume (in ml) to first sensation first constant sensation volume (FCSV), the volume that induces the need to defecate desire to defecate volume (DDV) and the maximum tolerated volume (DTV), using gradual inflation of the balloon. Rectal sensation thresholds (in ml of balloon distention) in patients with abnormal (reduced) sensation (> 2 out of 3 sensory parameters above the upper limit of normal were then recorded and analyzed per the London classification). This is finally followed by the Balloon Expulsion Test (BET) that measures the ability to expel a 60-ml balloon from the rectum within 60 s. Normal values for our laboratory used over the study period and in this analysis are as follows: maximal anal sphincter basal pressure: 85 mm Hg, maximal anal sphincter squeeze pressure: 245 mmHg, rectal sensation to balloon distention: 10–50 ml; and recto-anal inhibitory reflex (RAIR) threshold present and elicited with < 60 ml of balloon distention. All medications were discontinued for 24 h prior to HR-ARM except for the patients with Parkinson's disease and chronic neuropathic pain. For the purposes of this analysis, values outside those ranges were considered abnormal.

## WMC Protocol

The WMC (Smartpill; Medtronic, Sunnyvale, California, USA) is an ambulatory, non-invasive and non-radioactive diagnostic sensor that continuously samples intraluminal pH, temperature, and pressure, as it moves through the gastrointestinal tract [13]. Patients first ingested a meal to initiate postprandial motility after an overnight fast. The meal consisted of a SmartBar (260 kcal, 2% fat, 2-g fiber), followed by 120-ml water. Shortly after the meal, patient swallowed the capsule with 50-ml water. Patients were then released, and they were given the data receiver and a diary for recording bowel movements, food intake, sleep, and gastrointestinal symptoms. Physical restrictions included no strenuous activities, such as sit-ups, abdominal crunches, and prolonged aerobic activity (> 15 min), which could affect pressure measurements. Additionally, patients refrained the use of gastrointestinal medications that could affect motility (i.e., laxatives) or gastric pH (i.e., proton pump inhibitors). Patients were asked to fast for 6 h after capsule ingestion, after which they ingested a regular meal. This meal would allow for the evaluation of the fed response, which is the change in contractile pattern of the small bowel from a fasting to postprandial pattern. Patients were then instructed to continue their regular diet and routine and to return the data receiver and diary to our facility after 5 days. Downloaded data were analyzed using the display software (Medtronic, Sunnyvale, California, USA). All medications were discontinued for 5 days before and during the 5-day conduct of WMC, except for the patients with Parkinson's disease and chronic neuropathic pain. Normal colonic transit time (CTT) was a priori defined as < 59 h, while prolonged CTT was > 60 h.

## Analyses

We used the London classification that hierarchically examines for (a) the presence or absence of RAIR (areflexia), (b) any disorders of anal tone (maximal anal sphincter basal pressure) and contractility (maximal anal sphincter squeeze pressure, (c) disorders of anorectal coordination, and (d) disorders of rectal sensation to balloon distention (RST), specifically hypo- and hypersensitivity. BET was also analyzed and reported separately as positive (60-ml balloon expelled in a timely fashion, < 60 s) or negative. In our laboratory, normal values (ranges) for both men and women are as follows: recto-anal inhibitory reflex (RAIR) present, internal anal sphincter, 67–82 mmHg; external anal sphincter, 191–247 mmHg; rectal hypersensitivity, perception with < 10-ml balloon distention; and rectal hyposensitivity perception with > 40-ml balloon distention. Continuous variables were presented as median and interquartile range (IQR 25–75%) and categorical variables as percentages. For univariate analysis, Fisher's exact test or Pearson Chi-square test was performed as appropriate. Continuous variables were compared with the use of the Mann–Whitney *U* tests (Wilcoxon rank-sum test). All statistical analyses were performed using Stata version 14 (Stata Corp LLC, College Station, TX, USA). In all cases, $p \leq 0.05$ was considered significant.

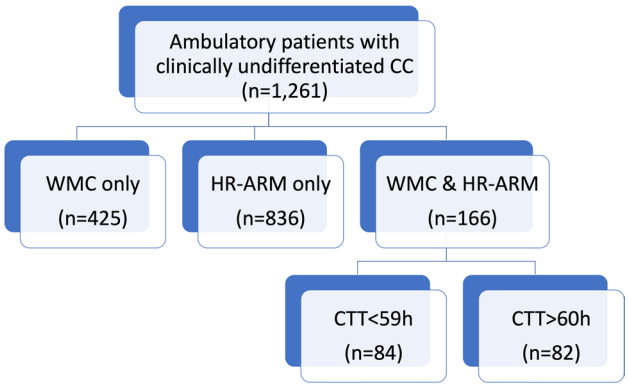


**Fig. 1** Diagram of the study flow. WMC wireless motility capsule, HR-ARM high-resolution anorectal manometry

## Results

The initial study cohort consisted of 1261 patients with clinically undifferentiated CC (Fig. 1). Of those, 425 only underwent WMC, while 836 patients only underwent HR-ARM, and they were excluded from study since their overall assessment remained incomplete and management decisions were made based on the results of the performed study without input from the other. Reasons for exclusion varied, ranging from lack of insurance authorization, technical inadequacy of either procedure, unwillingness to undergo testing, or inability to tolerate the procedure. The remaining 166 patients who received both technically satisfactory studies formed the final, analyzed study cohort, and they were divided into 84 who had normal CTT (normal transit) and 82 who had abnormal (prolonged) CTT (slow transit).

Demographically, there were some statistical differences between the two groups. Patients with normal transit were younger than those with slow transit ($p$ value 0.008) (Table 1). The normal CTT group ($n=84$) consisted of 40 women and 44 men, 71 Whites, 2 Hispanic, and 11 Asians, and they had a median age of 63 years (range 22–86). Their median reported disease duration was 2 years. The abnormal CTT group ($n=82$), consisted of 35 women and 47 men, 71 Whites, 4 Hispanics, and 7 Asians; their median age was 69 years (range 24–86). Their mean disease duration was 3 years ($p$ value 0.0155) (Table 1).

Figure 2 graphically depicts the median symptom scores for each interrogated variables (lower abdominal pain,

**Table 1** Patient demographics and other characteristics in the two study groups

| | Slow transit ($n=82$) | Normal transit ($n=84$) | $p$-value |
|---|---|---|---|
| Age median (IQR) | 69 (51–72) | 63 (60–74) | **0.008** |
| Sex | | | 0.523 |
| Female | 35 | 40 | |
| Male | 47 | 44 | |
| Background | | | 0.719 |
| Asian | 7 | 11 | |
| Hispanic | 4 | 2 | |
| White | 71 | 71 | |
| CTT (hours) | 82.5 (68–93) | 33 (16–43) | **0.0000** |
| CC duration (years) | 3 (2–8) | 2 (1–5) | **0.0155** |
| Abdominal pain | 0 (0–1) | 0 (0–1) | 0.3224 |
| Reduced defecation frequency | 2 (1–3) | 1 (0–2) | **0.0003** |
| Incomplete evacuation | 1 (0–2) | 1 (0–2) | 0.7266 |
| Straining | 2 (1–3) | 1 (1–2) | **0.0001** |
| Total symptom score | 6 (3–8) | 4 (2–6) | **0.0015** |

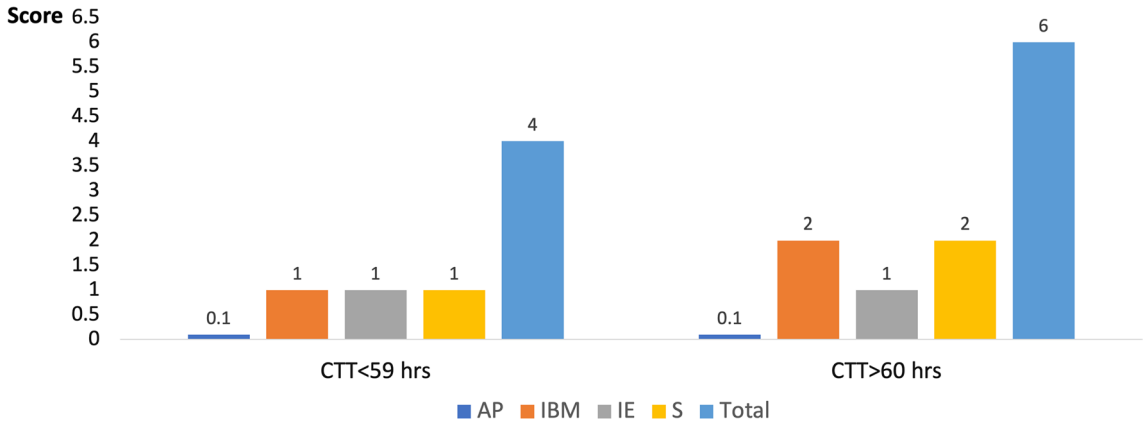


**Fig. 2** Median frequency and severity symptom scores in the two groups studied (see Methods). There were some statistically significant differences between the two groups of normal and prolonged colonic transit times (CTT) (see Table 1). Scores: 0 = none; 1 = Mild; 2 = Moderate; 3 = Severe. AP abdominal pain, IBM infrequent bowel movements, IE incomplete evacuation, S straining, and T total score (see Methods)

infrequent bowel movements, incomplete evacuation, and straining) in their various degrees of frequency and severity (0 = none; 1 = Mild; 2 = Moderate; 3 = Severe), as well as the median total scores in both groups. Symptom scores were different in the two groups (Table 1). In the normal group, the median total score was 4, while the abnormal CTT group had a median total score of 6 (Table 1). Reduced defecation frequency, straining, and total symptom scores were significantly different between the 2 groups.

Upon record review, underlying conditions or associated diagnoses that could potentially play a role in symptom induction at the time of initial presentation for CC were as follows: chronic depression on tricyclics ($n = 3$), chronic visceral and peripheral neuropathy ($n = 4$), Parkinson's disease ($n = 13$), opioid-induced constipation ($n = 2$), constipation-predominant irritable bowel syndrome (IBS-C; $n = 59$), diverticulosis ($n = 6$), chronic idiopathic constipation (CIC; $n = 32$), chronic intestinal pseudo-obstruction (CIPO; $n = 6$), progressive systemic sclerosis ($n = 2$), post-surgical ($n = 2$), rectocele ($n = 2$), diabetes mellitus ($n = 3$), recurrent volvulus ($n = 1$), recurrent small bowel bacterial overgrowth ($n = 17$), fecal impaction and overflow fecal incontinence ($n = 2$), and hypothyroidism ($n = 2$).

Table 2 depicts the % prevalence of HR-ARM abnormalities using the London classification and including the results of balloon expulsion test (BET) in the 166 patients studied and separated in two groups, those with normal (< 59 h), and those with abnormal (> 60 h) CTT. Of the entire cohort, there was only 1 patient exhibiting entirely normal CTT and HR-ARM. All others, in both groups, showed some abnormalities on HR-ARM by the London classification. Overall, we noted a high prevalence of anorectal dysfunction, regardless of CTT. Specifically, a minority of patients in each group, 13% in normal transit and 15% in slow transit exhibited areflexia (lack of RAIR) (NS) (Table 2). One key difference between the two groups was anal hypertonicity or increased anal sphincter tone that was significantly more prevalent (44%) in patients exhibiting normal CTT as opposed to 23% in the slow transit group ($p$ 0.004), a finding of questionable clinical implications. Other London classification parameters were noted at comparable frequencies among the normal transit and slow transit groups (Table 2).

Figure 3 provides information on part 3 of the London classification, specifically evidence of disorders of recto-anal coordination, which requires the use of both BET and HR-ARM. In the normal transit group, 15% had normal BET with dyssynergia and 6% without dyssynergia; failed BET with associated anorectal dyscoordination was seen in 31% of patients and 48% without dyssynergia. In the slow transit group, 7% had normal BET with dyssynergia and 12% without dyssynergia; failed BET with associated anorectal dyscoordination was seen in 43% of patients and 38% without dyssynergia. None of these minor and inconclusive London classification findings were statistically significantly different between the two groups.

Rectal hyposensitivity was seen in 59 (70%) of normal transit and 63 (77%) of slow transit patients (Table 2). Figure 4 depicts the rectal sensation thresholds (in ml of balloon distention) in patients with abnormal (reduced) sensation (rectal hyposensitivity; > 2 out of 3 sensory parameters above the upper limit of normal (see Methods), specifically, the FCSV, the DDV, and the DTV by the London classification), based on RST in those with normal ($n = 58$) and those with abnormal CTT ($n = 63$). In both groups, the remaining patients were assessed as having normal rectal sensation to balloon distention. There were no differences in rectal sensation thresholds between the two groups.

**Table 2** London classification findings in the two study groups

| Variables | Slow transit ($n = 82$) | Normal transit ($n = 84$) | $p$-value |
|---|---|---|---|
| Disorder of recto-anal inhibitory reflex | | | |
| Recto-anal areflexia | 12 (15%) | 11 (13%) | 0.774 |
| Disorders of anal tone and contractility | | | |
| High anal tone | 19 (23%) | 37 (44%) | **0.004** |
| Hypotonic and hypocontractile sphincter | 40 (49%) | 31 (37%) | 0.165 |
| Normotonic and hypocontractile sphincter | 7 (9%) | 3 (4%) | 0.155 |
| Disorders of rectal sensation | | | |
| Normal sensation | 19 (23%) | 25 (30%) | 0.336 |
| Hyposensitivity | 63 (77%) | 59 (70%) | 0.259 |
| Hypersensitivity | 0 | 0 | |
| Disorders of recto-anal coordination | | | |
| Failed BET | 66 (80%) | 66 (79%) | 0.760 |
| Dyssynergia | 41 (50%) | 39 (46%) | 0.089 |

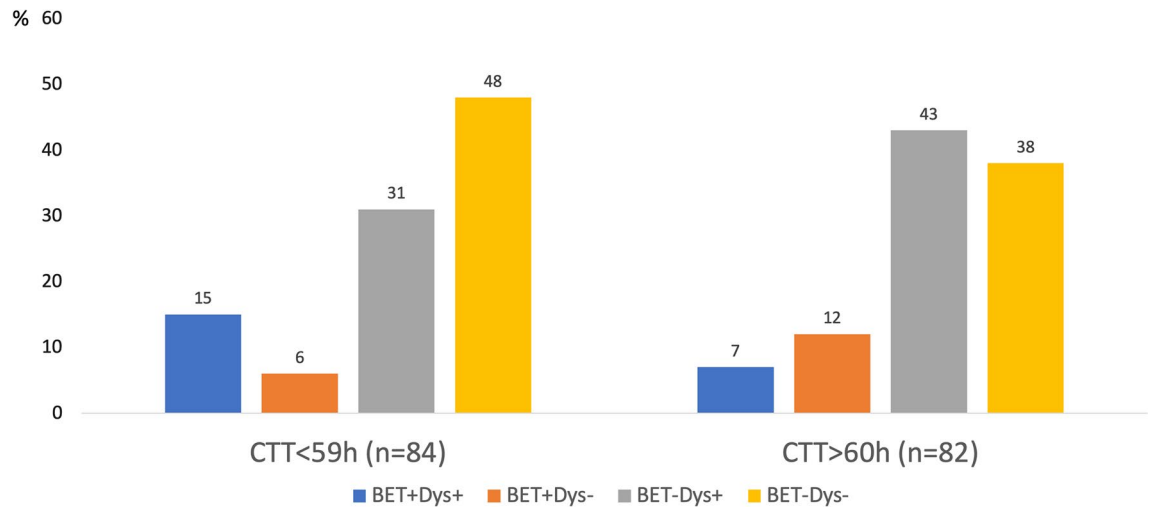


**Fig. 3** Disorders of anorectal coordination using the London classification based on the results of balloon expulsion test (BET) and HR-ARM during simulated defecation/push maneuver, in the two study groups, those with normal (< 59 h) and those with abnormal (> 60 h) colonic transit time (CTT). BET+: patient able to expel balloon, BET −: failed BET. Dys+: evidence of abnormal expulsion with dyssynergia. Dys −: no evidence of abnormal manometric pattern of anorectal evacuation. There were no statistically significant differences between the two groups of normal and prolonged CTT

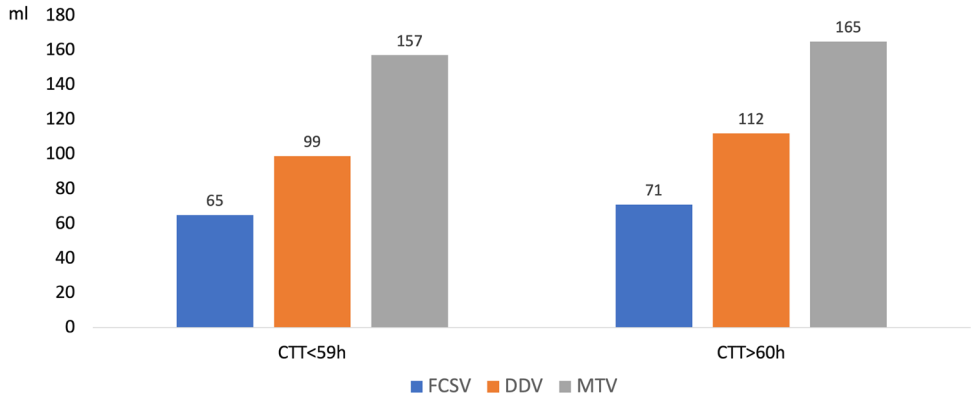


**Fig. 4** Rectal sensation thresholds (in ml of balloon distention) in patients with abnormal (reduced) sensation (> 2 out of 3 sensory parameters above the upper limit of normal; see Methods). FCSV first constant sensation volume, DDV desire to defecate volume, and DTV maximum tolerated volume (London classification), based on RST in those with normal ($n = 58$) and those with abnormal CTT ($n = 63$). In both groups, the remaining patients were assessed as having normal rectal sensation to balloon distention. Both groups exhibited similar rectal thresholds

## Discussion

This retrospective study, conducted on a community-based cohort suffering from chronic (> 6 months) constipation, examined the prevalence of HR-ARM abnormalities in the presence of normal (< 59 h) or prolonged (> 60 h) colonic transit by WMC testing. The key finding of our study was that, using the London classification, there is a high prevalence of anorectal dysfunction in ambulatory patients with clinically undifferentiated chronic constipation, regardless of colon transit time. Specifically, in patients with normal colon transit, 13% had inability to relax the anal sphincter, 44% showed elevation of anal sphincter pressure at rest, 70% had decrease in rectal sensation, and 79% failed balloon expulsion. In patients with prolonged colon transit, 15% exhibited inability to relax the anal sphincter, 23% showed elevation of anal sphincter pressure at rest, 77% had decrease in rectal sensation, and 80% failed balloon expulsion. Both groups exhibited similarly high prevalence of disorders of anorectal coordination, based on BET and HR-ARM during simulated defecation/push maneuver, ranging from 39 to 41%. These findings suggest that one should not make clinical decisions based on HR-ARM results alone, but instead, use

them in context, since alterations in anorectal motor and sensory function can co-exist with both normal and abnormal colonic transit times.

The IAPWG has emphasized that what is not normal on HR-ARM is not necessarily a reflection of disease and we will need more outcome studies that will be linked to clinical presentations and overcome existing disagreements. Our study findings support this notion, since only 1/166 patients exhibited normal CTT and HR-ARM. The London group has recommended a comprehensive pelvic floor evaluation to assess structure and function, such as endoanal ultrasound, defecography, rectal Barostat, or functional lumen imagine probe (FLIP). Further, the IAPWG has not recommended specific, quantitative reference limits, but they describe findings in accordance with the upper and lower limits of "normal," as we did in our study. The IAPWG also acknowledged that female sex, advanced age, and parity may have exerted a deleterious effect on anorectal motor and sensory dysfunction. Although we have no data on pregnancy and vaginal delivery in the females of our study, advanced age and female sex bared no importance on such dysfunctions, likely related to the ubiquitous prevalence of abnormalities in our selected cohorts, regardless of CTT [14].

Given the poor relationship between subjective symptoms and objective anorectal findings, anorectal function testing has been used for many years as a guide in clinical decision-making [15]. The recent consensus of the IAPWG is of significant impact as a new standard to be followed. Further, the hierarchical separation of the London classification into major abnormalities only seen in disease, minor and potentially of significance in symptomatic patients, or inconclusive would objectively facilitate characterization and individualize treatment of chronic constipation, fecal incontinence, and/or both and hopefully lead to better outcomes. We think that the present study provides another dimension, that of the relationship of the London classification findings to colonic transit, and its usefulness in decision-making. The patients in our cohort represented a challenging group since they could not be clinically differentiated, exhibiting variable degrees of abdominal pain (suggestive, using Rome IV criteria, of constipation-predominant irritable bowel syndrome (IBS-C), infrequent urge and bowel defecation, suggestive of chronic idiopathic constipation (CIC) and straining and incomplete evacuation, suggestive of evacuation disorder (ED)). Given the high prevalence of HR-ARM abnormalities irrespective of CTT, our cohort was ultimately managed by local means (gut-directed behavioral and pelvic floor therapy, enemas, and suppositories) when ED dominated, reassurance, antispasmodics, and fiber supplementation when CTT was normal, and combination strategies (oral osmotic and/or stimulant laxatives, behavioral and pelvic floor therapy, enemas and suppositories, and/or surgery) when CTT was dominant. Unfortunately, the retrospective nature of this study could not provide reliable outcome data on the efficacy or comparative effectiveness of such approaches, based on our testing [16, 17].

We have previously shown that in most clinical trials, a majority of patients treated with a newer agent remained constipated and that clinicians should anticipate a high probability that, with one of the newer treatments for constipation (such as with lubiprostone, methylnaltrexone, prucalopride, linaclotide, and naloxegol), a patient will remain constipated with persistent abdominal symptoms, and our current data revealing high proportion for ED, support this notion [18]. Surprisingly, recto-anal areflexia was a significant finding in our cohort. We did not find evidence of adult Hirschsprung's by biopsy and none of the patients underwent surgery. However, in such patients, there was more severe disease with chronic visceral and peripheral neuropathy, CIPO, Parkinson's disease, and diabetes, all with underlying elements of sensory impairment.

The key strength of our study is its community-based and pragmatic nature, derived from a stable cohort of patients followed by one clinician able to obtain high degree of granularity in their diagnosis, management, and follow-up, based on formal testing for their constipation. Yet, we would like to highlight several key weaknesses: (a) Retrospective in nature and small in sample size. As such, our current study will require further validation and confirmation prospectively, on more patients undergoing both WMC and HR-ARM, as part of a standardized protocol. (b) The select nature of our cohort. Our patients reported herein had more severe and refractory constipation that had not responded to medical therapy, mostly composed of various osmotic and stimulant laxatives, sometimes combined with enemas and/or suppositories. (c) Patient and physician preferences. The data presented herein could result from preselection of patients who ended up undergoing both WMC and HR-ARM based on ongoing diagnostic clinical uncertainty and during a short timeframe of less than 1 month from each other and < 3 months from the request time of the test. Mostly due to insurance non-authorization, many of our initial larger cohort did not have both studies performed. In other instances, positive findings in one or another study were considered adequate for decision-making and further management and the other study was not pursued. (d) Lack of well-validated clinical questionnaires for both chronic constipation and evacuation disorder that would link the frequency and severity of the clinical presentation to the laboratory findings. A multi-institutional study involving patients with a wider spectrum of indications (i.e., recurrent pseudo-obstructions, fecal impactions, overflow diarrhea), underlying etiologies (neuropathic or myopathic, post-operative), and symptom intensity and frequency and taking into consideration the effects of various concomitant drug therapies (carbidopa/levodopa, tricyclics, opioids,

etc.) in a precise fashion would be needed to address these deficiencies. Finally, (e) Lack of information on the durability and reproducibility of WMC and HR-ARM findings in these patients who were studied at the point of care and within 3 months' temporal proximity with each other. A previous study had shown that only a minority of patients who underwent repeat anorectal manometry as analyzed by the London Classification had stable manometric findings, raising questions regarding the validity of a single manometric measurement [19]. Further, the significance of the London classification findings varies, depending on their relative importance. For example, recto-anal areflexia is considered a major abnormality, while anal hypertension a minor one.

One clinically important question is the timing of the correction of the ED and its impact on CTT. For example, if significant anorectal dysfunction were present and untreated long term, this might have falsely prolonged CTT in some patients. Thus, it would be interesting to follow up CTT by WMC to learn if treated ED normalized transit. Unfortunately, we do not have longitudinal data demonstrating improvement of CTT upon correction of the ED, but we suspect it might be the case. ED is very prevalent and its correction (typically with pelvic floor physical therapy) often unsuccessful that would make such study difficult to implement and conclusions hard to reach.

The decision to proceed with subtotal colectomy in patients with STC requires thorough evaluation and judicious multidisciplinary approach, particularly in the CIPO patients whose clinical outcomes are typically inferior to those with isolated or mixed STC. In this study, we only had two patients in the cohort (a very small percentage) who underwent an elective—not urgent—subtotal colectomy (for STC, after failing physical therapy and laxatives) and another two who underwent sigmoid colectomy for volvulus. In none of these cases, we have f/u HR-ARM and WMC data. In general, slow colonic transit by WMC does not mandate colectomy for the patients in whom combinations of laxatives, pelvic floor physical therapy, and treatment of underlying disorders can adequately control symptoms.

In summary, this retrospective study raises some provocative questions about the interrelationship between WMC and HR-ARM parameters that will need to be addressed in a larger prospective trial before we can depend on the specificity and utility of these parameters in the assessment and clinical decision-making in patients with CC and associated functional anorectal symptoms. More work will also be needed to demonstrate the value of such measurements as surrogate markers of clinical response or as a response to gut behavioral and pelvic physical therapy or a particular pharmacologic or surgical intervention.

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## Declarations

**Conflict of interest** The authors declare no competing interests

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