Original Article

Rectosigmoid Localization of Radiopaque Markers for Identifying Defecation Disorders in Patients With Chronic Constipation: A Retrospective Cohort Study

Tatsuya Abe,[1]* Masao Kunimoto,[1] Yoshikazu Hachiro,[1] Kei Ohara,[1] Mitsuhiro Inagaki,[1] and Masanori Murakami[2]

Departments of [1]Proctology and [2]Gastroenterology, Kunimoto Hospital, Akebono, Asahikawa, Japan

Background/Aims

Defecation disorders (DD) are part of the spectrum of chronic constipation with outlet obstruction. Although anorectal physiologic tests are required for the diagnosis of DD, these tests are not available in many institutions. This study aims to investigate the predictivity of DD using rectosigmoid localization of radiopaque markers in a colonic transit study.

Methods

A total of 169 patients with refractory constipation with a mean age of 67 years were studied. All patients underwent anorectal manometry, a balloon expulsion test, and a colonic transit study. Barium defecography was performed if needed. The relationship between DD diagnosed by these anorectal tests and the rectosigmoid accumulation of markers was examined.

Results

Seventy-nine (46.7%) patients were identified to have DD based on anorectal test combinations. Rectosigmoid accumulation of markers was observed in 39 (23.1%) patients. The sensitivity and positive predictive value of rectosigmoid accumulation for identifying DD were 31.6% and 64.1%, respectively. Rectosigmoid accumulation provided poor discrimination of DD from normal transit constipation, at a specificity of 82.1% but with a sensitivity of only 10.6%. In discriminating DD from slow transit constipation, rectosigmoid accumulation was found to be useful with a positive likelihood ratio of 5.3.

Conclusions

Rectosigmoid accumulation of markers can differentiate DD from slow transit constipation. However, non-rectosigmoid accumulation does not exclude the presence of DD.
(J Neurogastroenterol Motil 2021;27:419-425)

Key Words

Biofeedback; Constipation; Defecation; Defecography; Manometry

*Correspondence: Tatsuya Abe, MD, PhD
Department of Proctology, Kunimoto Hospital, 1-7 Akebono, Asahikawa 0700061, Japan
Tel: +81-166252241, Fax: +81-166231726, E-mail: t-abe@cf6.so-net.ne.jp

ⓒ 2021 The Korean Society of Neurogastroenterology and Motility
J Neurogastroenterol Motil, Vol. 27 No. 3 July, 2021
www.jnmjournal.org

419

Introduction

Functional constipation is a common disorder that is classified into 3 large categories: slow transit constipation (STC), normal transit constipation (NTC), and defecation disorders (DD).[1,2] DD is common in patients with medically refractory chronic constipation (CC) and is characterized by impaired rectal evacuation resulting from increased resistance to evacuation and/or inadequate rectal propulsive forces. Various terms including anismus, dyssynergic defecation, pelvic floor dyssynergia, obstructive defecation, and outlet obstruction have been used to describe DD.[3-5] It is important to discriminate patients with DD from those with other types of CC, as those with DD have been shown to benefit from biofeedback therapy.[6]

Excessive straining, feeling of incomplete evacuation, and digital facilitation of bowel movements are symptoms related to DD, but these symptoms may also occur in patients with STC without DD. Several studies have advocated that no particular symptoms were useful in recognizing patients with DD.[7,8] Thus, the diagnosis of DD should depend on physiologic findings by means of anorectal testing.[3] In diagnostic guidelines, anorectal manometry (ARM) and the rectal balloon expulsion test (BET) are initially recommended in identifying DD, followed by defecography when ARM and BET results are equivocal or do not concur with the clinical impression.[3,9,10] However, these anorectal tests are not available in many institutions.

In Western countries, colonic transit studies (CTSs) using radiopaque markers are routinely used in clinical practice to evaluate patients with CC. The most commonly used techniques include a single ingestion of markers with an abdominal X-ray after 3 days[11-13] or a serial ingestion of markers over 3 days with an X-ray on the fourth day.[14,15] Because a CTS is simple, safe, and inexpensive, clinicians frequently use rectosigmoid (RS) localization of markers or regional colon transit as an alternative for anorectal tests. However, the role of CTS in diagnosing DD remains controversial. Some consensus guidelines suggest that marker accumulation in RS can help differentiate DD from STC.[16,17] In the latest guideline, a CTS result is no longer advocated as a diagnostic criterion for DD.[3]

Therefore, we attempt to reconfirm the relationship between marker location and the constipation subtypes. Moreover, we hypothesized that marker accumulation in RS would correlate with DD diagnosed by anorectal tests. This study aims to establish a simple method using a CTS to predict the possibility of DD.

Materials and Methods

Study Design

This retrospective, observational cohort study was based on the medical records of patients who were referred to the anorectal physiology unit in our hospital for refractory constipation. All processes of this study were approved by the Institutional Review Board of our hospital (Approval code: K11-002), and written informed consent to perform the tests and use the test results was obtained from all patients.

Study Participants

We assembled a retrospective cohort consisting of all adults ($\geq$ 20 years) who met the Rome diagnostic criteria for functional constipation[5] and underwent ARM, a BET, and CTS between January 2011 and December 2015. Patients were excluded if they had symptomatic anorectal abnormalities, such as anal stricture, rectocele, and rectal prolapse detected by proctologic examination or defecography. Patients with small rectoceles or rectal intussusceptions who were able to expel contrast in defecography were not excluded. Prior to the physiologic tests, a questionnaire regarding various CC symptoms based on the Rome criteria and Cleveland Clinic Constipation Score (CCCS)[18] was conducted to all patients.

Functional Studies

All patients underwent ARM, a BET, and CTS. Barium defecography (BD) was performed if the results of those tests were discrepant or differed from the clinical impression. These tests were performed by the same physicians while using the same devices during the study period. Dyssynergic patterns on ARM and impaired evacuation on a BET or BD were defined by the proposed diagnostic criteria for DD.[4] Details of each test are described below.

Colonic transit study

All patients ingested a Sitzmarks capsule (Konsyl Pharmaceuticals, Easton, MD, USA) containing 20 markers. The combination of drugs already used for the treatment of constipation was allowed. The CTS was assessed using the method by Bouchoucha et al,[12] where an abdominal X-ray was obtained 72 hours after ingestion. Retention of 8 or more markers on imaging was defined as STC, and retention of less than 8 markers was defined as NTC. Localization of markers on an X-ray was done by identifying body structures as described in the study by Arhan et al[19] (Fig. 1).
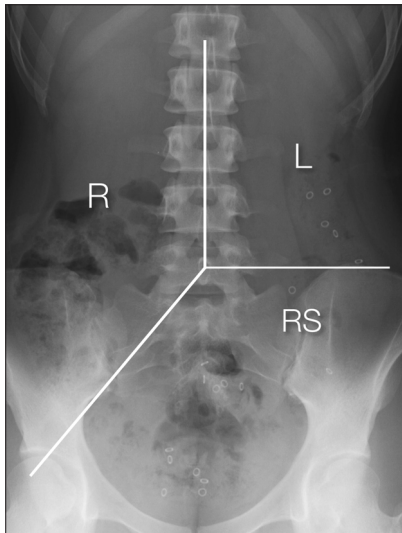
Figure 1. Colonic segments on an abdominal film. Spinal processes and imaginary lines from the fifth lumber vertebra to the right pelvic outlet and left iliac crest serve as landmarks and defined projection zones of the right (R), left (L), and rectosigmoid (RS) colon.

Anorectal manometry

ARM was performed using a one-channel, solid-state catheter with the patient in the left lateral position. The patient was instructed to bear down (push), as if trying to defecate, and staff recorded intrarectal pressure and anal pressure during the push. Manometric findings were regarded as pathologic findings when there was one of the following dyssynergic patterns according to the Rao classification[4]: sufficient rise in rectal pressure ($\geq$ 45 mmHg) with paradoxical rise in anal pressure (type I), insufficient rise in rectal pressure ($<$ 45 mmHg) with paradoxical rise in anal pressure (type II), sufficient rise in rectal pressure with incomplete decrease ($<$ 20%) in anal pressure (type III), or insufficient rise in rectal pressure with incomplete decrease in anal pressure (type IV).

Balloon expulsion test

Following ARM, a 4-cm long latex balloon filled with 25 mL of air was placed in the patient's rectum. Thereafter, the patient was asked to expel the balloon. Failure to expel the balloon within $<$ 60 seconds was considered impaired rectal evacuation.[4]

Barium defecography

A suppository was used to empty the rectum before defecography. The patient was seated on a portable plastic toilet, and approximately 150 mL of diluted barium paste was injected into the patient's rectum. Next, the patient was asked to start defecating, and fluoroscopy during evacuation was recorded on video. Retention of $\geq$ 50% contrast was defined as impaired evacuation.[4]

Diagnosis of Defecation Disorders

DD was diagnosed according to the Rome criteria for functional DD.[5] The Rome criteria require evidence of at least 2 of the following: (1) the presence of a dyssynergic pattern (types I-IV) on ARM, (2) inability to expel a balloon, and (3) $\geq$ 50% retention of barium during defecography.

Main Outcome Measures

The primary outcome measure was RS localization of residual markers on day 3 of abdominal X-ray. The accumulation rate of markers was calculated as the ratio of the number of markers localizing in the RS colon among all the remaining markers on the film. Receiver operating characteristic (ROC) curves were used to find the diagnostic utility and optimal cutoffs of the RS accumulation rate. We stratified our cohort into patients with RS accumulation based on the ROC curves and those without RS accumulation.

Statistical Methods

Categorical variables are reported as frequencies and percentages, whereas continuous variables are reported as means and SD. We determined the correlation between RS accumulation and the individual anorectal tests or DD based on the Rome criteria, using sensitivity, specificity, positive and negative predictive values, and likelihood ratios (LR). LRs $\geq$ 5.0 or $\leq$ 0.2 were considered clinically relevant. All statistical analyses were performed using EZR software version 1.11 (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

Results

Patient Demographics

The study included 97 women (57.4%) and 72 men (42.6%) aged 22-92 years (mean age $\pm$ SD [67.2 $\pm$ 16.3] years). Patient characteristics and individual CCCS symptom domains are shown in Table 1. The breakdown of immediate pharmacotherapy for constipation was 98 cases of stimulant laxatives, 49 cases of osmotic laxatives, and 25 cases of enemas or suppositories and others (overlapping).

Findings of the Colonic Transit Study

At least 1 marker remained in 96 (56.8%) patients, whereas

in 73 (43.2%), no marker was seen on the abdominal film. There was a mean of 6.85 markers present on the film, and 66 (39.1%) patients had STC (≥ 8 markers remaining). There was a mean of 4.31 markers present in the RS colon, and 86 (50.9%) patients had at least 1 marker in the RS colon.

Findings of the Anorectal Tests

The manometric characteristics and prevalence of each dyssynergic pattern are shown in Table 2. A dyssynergic pattern was observed in 158 (93.5%) patients, and the prevalence of type 1 dys-

synergia was considerably high. The BET result was positive in 75 (44.4%) patients, and these patients were categorized as having impaired rectal evacuation. BD was performed in 83 (49.1%) patients, of whom 44 (53.0%) patients were unable to expel ≥ 50% of the barium. These patients were also categorized as having impaired evacuation (Table 3). Incidentally, BD also revealed a small asymptomatic rectocele in 7 patients.

Diagnosis of Defecation Disorders

Based on the findings of anorectal tests, 79 of 169 (46.7%) patients were identified to have DD. There were no significant differences in the prevalence of DD and positive findings on anorectal tests between patients with NTC and those with STC (Table 3).

Receiver Operating Characteristic Analysis of Rectosigmoid Accumulation

For the rate of RS accumulation, a cutoff of ≥ 80% of markers was most useful (sensitivity, 31.6%; specificity, 83.3%) in discrimi-

Table 1. Characteristics of the Study Population (N = 169)

Variable	Value
Age (yr)	67.2 (16.3)
Female sex (n [%])	97 (57.4)
Height (cm)	157.8 (8.9)
Weight (kg)	57.2 (11.8)
Stool frequency (time/wk) (n [%])	
≥ 3	89 (52.7)
≥ 1 to < 3	60 (35.5)
< 1	20 (11.8)
Bristol stool form scale score (n [%])	
1-2	91 (53.8)
3-5	57 (33.7)
6-7	21 (12.4)
Immediate pharmacotherapy for constipation (n [%])	141 (83.4)
Cleveland Clinic Constipation Score	11.5 (4.1)
Frequency of bowel movement	0.9 (1.1)
Painful evacuation effort	1.8 (1.2)
Feeling incomplete evacuation	2.4 (1.2)
Abdominal pain	1.0 (1.2)
Minutes in lavatory per attempt	1.1 (1.1)
Assistance for defecation	1.4 (0.7)
Unsuccessful attempts per 24 hr	1.2 (0.9)
Duration of constipation (yr)	1.8 (1.5)

Values are presented as mean (SD) unless specified otherwise.

Table 2. Anorectal Manometric Characteristics and Distribution of Manometric Pattern of the Study Population (N = 169)

Variable	Value
Anorectal pressure (mmHg)	
Anal pressure at rest	51.2 (22.7)
Anal pressure at simulated evacuation	80.6 (38.5)
Rectal pressure at simulated evacuation	59.6 (24.2)
Rectoanal gradient at simulated evacuation	−21.0 (32.2)
Manometric patterns (n [%])	
Normal	4 (2.4)
Type I dyssynergia	101 (59.8)
Type II dyssynergia	31 (18.3)
Type III dyssynergia	19 (11.2)
Type IV dyssynergia	7 (4.1)
Unclassified	7 (4.1)

Values are presented as mean (SD) unless specified otherwise.

Table 3. Proportion of Positive Findings on Anorectal Tests in Patients With Normal and Slow Transit Constipation

Positive findings (positive patients/total patients)	Colonic transit study results		P-value
	NTC (n = 103)	STC (n = 66)	
Dyssynergic pattern on ARM (158/169)	96 (93.2)	62 (93.9)	0.850
Failure to expel the balloon during a BET (75/169)	45 (43.7)	30 (45.5)	0.822
Impaired evacuation (< 50% contrast) on BD (44/83)	32/55 (58.2)	12/28 (42.9)	0.186
Meets the Rome criteria for DD (79/169)	47 (45.6)	32 (48.9)	0.717

NTC, normal transit constipation; STC, slow transit constipation; ARM, anorectal manometry; BET, balloon expulsion test; BD, barium defecography; DD, defecation disorders.
Values are presented as n (%) unless specified otherwise.

Table 4. Relationship Between Rectosigmoid Accumulation and the Findings of Anorectal Tests

Positive findings on anorectal tests	RS accumulation		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	+LR	−LR
	≥ 80% (n = 39)	< 80% (n = 130)						
Dyssynergic pattern on ARM	36/39	122/130	22.8	72.7	92.3	6.2	0.84	1.06
Impaired evacuation on a BET	23/39	52/130	30.7	83.0	59.0	60.0	1.81	0.83
Impaired evacuation on BD	9/16	35/67	20.5	82.1	56.3	47.8	1.15	0.97
DD met the Rome criteria	25/39	54/130	31.6	84.4	64.1	58.5	2.03	0.81
Discriminating DD from NTC	5/15	42/88	10.6	82.1	33.3	52.1	0.59	1.09
Discriminating DD from STC	20/24	12/42	62.5	88.2	83.3	74.1	5.31	0.43

RS, rectosigmoid; PPV, positive predictive value; NPV, negative predictive value; +LR, positive likelihood ratio; −LR, negative likelihood ratio; ARM, anorectal manometry; BD, barium defecography; DD, defecation disorders; NTC, normal transit constipation; STC, slow transit constipation.

nating patients with DD from those without DD. The corresponding area under the ROC curve was 0.514.

Identification of Defecation Disorders by Rectosigmoid Accumulation

RS accumulation (≥ 80%) was observed in 39 (23.1%) patients: 25 of 79 patients with DD and 14 of 90 patients without DD. No single anorectal test result correlated with RS accumulation (Table 4). The sensitivity and positive predictive value of RS accumulation for identifying DD were 31.6% and 64.1%, respectively. In determining DD from NTC at a specificity of 82.1%, the sensitivity was only 10.6%. However, for discriminating DD from STC at a sensitivity of 62.5%, the specificity was 88.2%, and it was found to be useful for predicting DD, with a +LR of 5.31 (Table 4).

Discussion

In this study, we found that RS accumulation was useful in discriminating DD from STC, but it did not help in distinguishing between DD and NTC.

The essential reason why RS accumulation failed to determine DD from NTC in this study was that no marker was retained in 70.9% of NTC cases. Prediction of DD by RS accumulation is impossible in cases where no marker is retained. Thus, most of the DD cases with NTC were missed, and the sensitivity was extremely low at 10.6%. On the other hand, since at least 8 markers were retained in patients with STC, DD could be identified based on RS accumulation. However, even in patients with STC, DD can be missed where most markers have not yet reached RS due to extremely slow transit. As a result, the sensitivity to detect DD from STC was still insufficient (62.5%).

Despite the frequent use of a CTS in clinical practice, there is
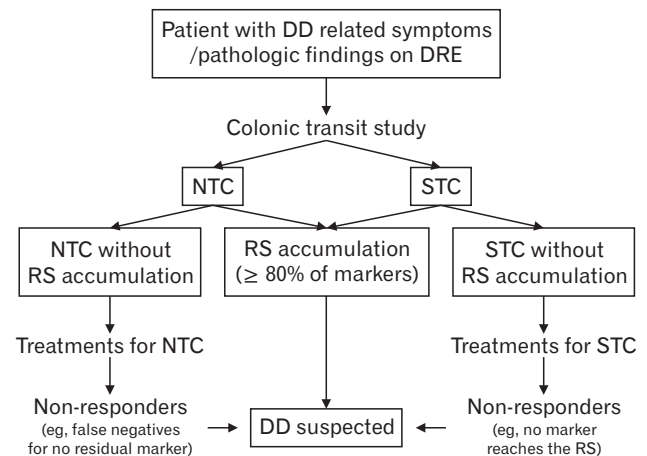

Figure 2. Our diagnostic algorithm of defecation disorders using a colonic transit study. DD, defecation disorders; DRE, digital rectal examination; NTC, normal transit constipation; STC, slow transit constipation; RS, rectosigmoid colon.

little evidence that RS localization of markers is associated with the presence of DD. Staller et al[20] reported that there was no significant correlation between patients with complete accumulation of markers in RS and those with DD defined by anorectal tests. Grotz et al[7] also reported that RS transit delay was not helpful for discriminating DD from NTC as well as DD from STC. Moreover, Cowlam et al[13] reported that neither RS transit time nor the geometric center of markers could discriminate patients with DD. On the other hand, Nullens et al[21] showed that regional (descending and RS colon) transit profiles can differentiate DD from STC.

As mentioned earlier, the drawback of a CTS is that it misses DD when the residual marker is zero or when the markers do not even reach the RS colon. In order to increase the sensitivity of detecting DD by a CTS, 2 methods can be used: use different types

of markers for a few consecutive days and take additional abdominal films. However, our aim is to establish a simple method, rather than a research tool, that can be applied in routine clinical practice. We believe that a single-capsule technique with a single abdominal film is the best method in terms of simplicity, cost, patient compliance, and radiation exposure.

With reference to these findings, we propose the following CTS diagnostic algorithm for predicting patients with DD (Fig. 2). A patient with suggested DD based on clinical symptoms or digital rectal examination findings is considered to have DD if any of the following patterns are shown: (1) NTC patients without RS accumulation do not respond to treatments for NTC (eg, false negatives for no residual marker), (2) NTC or STC patients with RS accumulation, and (3) STC patients without RS accumulation do not respond to treatments for STC (eg, no marker reaches the RS).

Among patients with refractory constipation with no underlying organic cause, assessments of anorectal function are initially recommended because DD may be responsible for delayed colonic transit.[3,4] Using the aforementioned protocol, the presence of DD can be inferred by performing a CTS in general clinics. As a result, clinicians can make a timely diagnosis to provide an appropriate treatment or optimize referral to specialized centers.

This study has several strengths. The sample size was comparable to other reports. Clinical symptoms and results of the anorectal tests were evaluated using validated and standardized techniques and interpreted using established criteria. The limitations of this study include its retrospective, single-center, observational design and the low accuracy of ROC analysis due to the low sensitivity of RS accumulation.

In conclusion, the appearance of RS accumulation weakly suggests the presence of DD. However, a CTS is not suitable for the exclusion diagnosis of DD because there are many false negatives, particularly in NTC. When clinicians use a CTS to recognize the mechanism of its low sensitivity, it may be helpful for identifying subgroups of patients with CC.

References

1. Lembo A, Camilleri M. Chronic constipation. N Engl J Med 2003;349:1360-1368.
2. Lacy BE, Mearin F, Chang L, et al. Bowel disorders. Gastroenterology 2016;150:1393-1407.
3. Ward A, Bharucha AE, Cosman BC, Whitehead WE. ACG clinical guideline: management of benign anorectal disorders. Am J Gastroenterol 2014;109:1141-1157.
4. Rao SS, Patcharatrakul T. Diagnosis and treatment of dyssynergic defecation. J Neurogastroenterol Motil 2016;22:423-435.
5. Rao SS, Bharucha AE, Chiarioni G, et al. Functional anorectal disorders. Gastroenterology 2016;150:1430-1442, e4.
6. Rao SS, Seaton K, Miller M, et al. Randomized controlled trial of biofeedback, sham feedback, and standard therapy for dyssynergic defecation. Clin Gastroenterol Hepatol 2007;5:331-338.
7. Grotz RL, Pemberton JH, Talley NJ, Rath DM, Zinsmeister AR. Discriminant value of psychological distress, symptom profiles, and segmental colonic dysfunction in outpatients with severe idiopathic constipation. Gut 1994;35:798-802.
8. Glia A, Lindberg G, Nilsson LH, Mihocsa L, Akerlund JE. Clinical value of symptom assessment in patients with constipation. Dis Colon Rectum 1999;42:1401-1408; discussion 1408-1410.
9. Bharucha AE, Wald A, Enck P, Rao S. Functional anorectal disorders. Gastroenterology 2006;130:1510-1518.
10. Bharucha AE, Pemberton JH, Locke GR 3rd. American Gastroenterological Association technical review on constipation. Gastroenterology 2013;144:218-238.
11. Hinton JM, Lennard-Jones JE, Young AC. A new method of studying gut transit times using radiopaque markers. Gut 1969;10:842-847.
12. Bouchoucha M, Devroede G, Arhan P, et al. What is the meaning of colorectal transit time measurement? Dis Colon Rectum 1992;35:773-782.
13. Cowlam S, Khan U, Mackie A, Varma JS, Yiannankou Y. Validity of segmental transit studies used in routine clinical practice, to characterize defaecatory disorder in patients with functional constipation. Colorectal Dis 2008;10:818-822.
14. Metcalf AM, Phillips SF, Zinsmeister AR, MacCarty RL, Beart RW, Wolff BG. Simplified assessment of segmental colonic transit. Gastroenterology 1987;92:40-47.
15. Kim ER, Rhee PL. How to interpret a functional or motility test - colon transit study. J Neurogastroenterol Motil 2012;18:94-99.
16. Lin HC, Prather C, Fisher RS, et al. Measurement of gastrointestinal transit. Dig Dis Sci 2005;50:989-1004.
17. Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology 2006;130:1480-1491.
18. Agachan F, Chen T, Pfeifer J, Reissman P, Wexner SD. A constipation scoring system to simplify evaluation and management of constipated patients. Dis Colon Rectum 1996;39:681-685.
19. Arhan P, Devroede G, Jehannin B, et al. Segmental colonic transit time. Dis Colon Rectum 1981;24:625-629.

20. Staller K, Barshop K, Ananthakrishnan AN, Kuo B. Rectosigmoid localization of radiopaque markers does not correlate with prolonged balloon expulsion in chronic constipation: results from a multicenter cohort. Am J Gastroenterol 2015;110:1049-1055.

21. Nullens S, Nelsen T, Camilleri M, et al. Regional colon transit in patients with dys-synergic defaecation or slow transit in patients with constipation. Gut 2012;61:1132-1139.