Fecal Evacuation Disorder Among Patients With Solitary Rectal Ulcer Syndrome: A Case-control Study

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Background/Aims
Data on frequency of fecal evacuation disorder (FED) among patients with solitary rectal ulcer syndrome (SRUS), hitherto an enigmatic condition, are scanty. Moreover, most such studies had limitations due to small sample size and lack of inclusion of healthy controls (HC).

Methods
Forty patients with SRUS underwent symptom assessments, sigmoidoscopy, anorectal manometry, defecography, balloon expulsion test (BET); endoscopic ultrasound (EUS) of anal sphincter complex was performed in a subgroup. Physiological tests (anorectal manometry and BET) were also performed in 19 HC.

Results
Patients with SRUS (26/40 male, age 37 [18-80] years) more often had FED than HC (10/19 male, age 43 [25-72] years) as shown by weight needed to expel the balloon (300 [0-700] g vs. 100 [0-400] g; P = 0.006), a trend towards abnormal BET (need of > 200 g weight for expulsion) (21/40 [53%] vs. 5/19 [26%], P = 0.058) and impaired anal relaxation (14/40 [35%] vs 2/19 [10.5%]; P = 0.048). Using Rome III criteria, most patients with SRUS reported having chronic constipation (36/40 [90%]) in spite of having normal (Bristol stool type IV, 21/40 [53%]) and diarrheal (types V, VI, VII, 6/40 [20%]) stool forms (Asian classification). SRUS patients more often (17/40 [43%]) had functional defecation disorder (Rome III criteria). Patients with SRUS with abnormal BET had thicker internal anal sphincter than those without (3.9 [3.4-7.0] mm vs 2.8 [2.0-4.0] mm; P = 0.01).

Conclusions
FED was commoner among patients with SRUS as evidenced by abnormal BET and sphincter relaxation. Those with abnormal BET had thicker internal sphincter on EUS than those without.

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Key Words
Constipation; Defecation; Dyschezia; Functional gastrointestinal disorders, anal sphincter
Introduction

Solitary rectal ulcer syndrome (SRUS) is a disorder affecting all ages and presents with rectal bleeding, mucorrhea, tenesmus and feeling of incomplete evacuation. It may be considered as part of spectrum of diseases like anterior mucosal prolapse, solitary rectal ulcer (SRU) and full thickness rectal prolapse. Pathogenesis of SRUS is not known. Mucosal ischemia was proposed to be an etiological factor in the past. Recently, fecal evacuation disorder (FED; also known as functional defecation disorder) has been proposed to be an important factor in the pathogenesis of SRU in a few uncontrolled studies on small number of patients. Some studies showed symptomatic benefit, ulcer healing and improvement in mucosal blood flow following biofeedback in patients with SRUS.

Accordingly we undertook a prospective case-control study to evaluate the frequency of fecal evacuation disorder among patients with SRUS compared to healthy control (HC) using anorectal manometry (ARM) and balloon expulsion test (BET). In a subgroup of patients, we also evaluated anal sphincter complex using endoscopic ultrasonography (EUS). In addition, clinical symptoms of patients with SRUS and defecography were also evaluated.

Materials and Methods

Forty patients with SRUS diagnosed by proctosigmoidoscopy and histopathology during a two and a half year period (from November 2011 to February 2014) were included. All patients underwent clinical evaluation, ARM, BET and defecography. In a subgroup of patients, we also evaluated anal sphincter complex using endoscopic ultrasonography (EUS). In addition, clinical symptoms of patients with SRUS and defecography were also evaluated.

Clinical Evaluation

Patients were evaluated clinically using a standard questionnaire including 8 categories of general gastrointestinal symptoms (predominant stool form and frequency, bleeding per rectum, mucus discharge, tenesmus, feeling of incomplete evacuation, manual evacuation and straining while defecation). Predominant stool form (off laxative period) was recorded using Bristol stool form chart with pictorial representation and descriptor. The laxative consumption score per week (0: no laxatives, 1: high fiber diet ± additional fiber supplement, 2: oral laxatives, 3: enemas, polyethylene glycol electrolyte solution or rectal suppositories) was calculated.

Anorectal Manometry

Each patient underwent ARM using a water perfusion manometry system (RMH, Melbourne, Australia) using a standard technique. A sixteen-lumen manometry catheter was used. The manometry catheter was inserted deep inside the rectum with the patient in the left lateral position. The catheter was subsequently pulled down slowly to be positioned at the high pressure zone of the sphincter with a few upper ports in the rectum and a few lower ports outside the anus. The lengths of the sphincter zone and resting sphincter pressure were estimated from an average of length and pressure data obtained. Subsequently the patient was asked to bear down and residual anal sphincter pressure was estimated. Rise in sphincter pressure on squeezing was measured. Subsequently, the balloon, mounted on the catheter tip positioned inside the rectum was inflated with an incremental volume of air (20, 40, 60 mL and so on). Recto-anal inhibitory reflex (RAIR) and rectal sensations (e.g., first feeling of distension, urge to pass stool and maximum tolerable limit) were also assessed during balloon inflation.

Analysis of Manometry Signal

The ARM signal was analyzed using Trace 1.2.1 software. The data were interpreted based on the standard criteria. A resting pressure of > 68 mmHg, squeeze pressure > 164 and length of anal high pressure zone > 3.6 cm in females and > 4 cm in males were considered as abnormal (high). Threshold volume for first sensation at > 20 mL in both gender, an urge to defecate at > 80 mL in male and > 60 mL in female and maximum tolerable volume of > 126 mL were taken as abnormal (high). Some of these cut-off values were based on a study from South Korea on 54 healthy subjects. The percentage of anal relaxation was calculated from the following equation.

\[
\frac{\text{Anal resting pressure} - \text{anal residual pressure}}{\text{Anal resting pressure}} \times 100
\]
Balloon Expulsion Test

A latex balloon, tied on the tip of a thin catheter was placed inside the rectum and filled with 60 mL water. The patient was asked to expel this while lying in left lateral position. If the balloon could be expelled without or with addition of weight of up to 200 g on the other end of the catheter, it was considered normal.17

Defecography

Defecography was performed after a cleansing rectal enema according to a standard technique.18,19 About 150-200 mL of thick barium paste was introduced inside the rectum. Lateral radiographs were obtained during rest, squeezing and defecation while the patient was sitting on a defecation chair.20

Endoscopic Ultrasonography

EUS was performed using a radial echoendoscope at 12 MHz frequency. Once the echoendoscope was inserted 3-4 cm inside the anal canal, the balloon mounted on its tip was inflated with water. Pubo-rectal sling was identified as a semicircular hypo-echoic structure. On pulling the echoendoscope down, internal and external anal sphincters (IAS and EAS) were identified as hypo- and hyper-echoic circular structures (Figure E and F), respectively. Thickness of these muscles was measured. Thickness of IAS and EAS of greater than 3 and 9 mm, respectively was considered abnormal.21-24

Functional defecation disorder was diagnosed according to the Rome III criteria if patient had chronic constipation and any 2 of the 3 physiological tests were abnormal; the test abnormalities included: (1) evidence of impaired evacuation, based on BET or imaging; (2) inappropriate contraction of pelvic floor muscles (i.e., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry or imaging; or (3) inadequate propulsive forces assessed by manometry or imaging.25

Statistical Methods

Qualitative data were presented as proportion and the continuous data were presented as median (range). Categorical variables were analyzed using Chi-squared test and Fisher’s exact test.
Table 1. Bristol Stool Score and Endoscopic Finding With Solitary Rectal Ulcer Syndrome

| Type of Stool | Bristol stool score | No. of patients (%) (n = 40) |
|---------------|---------------------|-------------------------------|
| Constipation  | Type 1              | 3 (7)                         |
|               | Type 2              | 4 (10)                        |
|               | Type 3              | 4 (10)                        |
| Normal        | Type 4              | 21 (53)                       |
| Diarrhea      | Type 5              | 6 (15)                        |
|               | Type 6              | 2 (5)                         |
|               | Type 7              | 0 (0)                         |

Endoscopic finding

| Endoscopic finding | No. of patients (%) (n = 40) |
|--------------------|-------------------------------|
| Rectal ulcer       |                               |
| No rectal ulcer    | 10 (25)                       |
| Solitary lesion    | 23 (57)                       |
| Two                | 3 (8)                         |
| Three              | 2 (5)                         |
| Multiple lesion    | 2 (5)                         |
| Size of rectal ulcer|                             |
| < 0.5 cm           | 14 (35)                       |
| 0.5-1 cm           | 7 (17.5)                      |
| 1-2 cm             | 2 (5)                         |
| 2.5 cm             | 4 (10)                        |
| > 5 cm             | 3 (7.5)                       |
| Hemorrhoids        |                               |
| Gr I               | 6 (15)                        |
| Gr II              | 3 (7.5)                       |
| Gr III             | 1 (2.5)                       |

Laxative consumption score per week

| Laxative consumption score per week | No. of patients (%) | No. with abnormal BET (%) |
|------------------------------------|---------------------|----------------------------|
| No laxative (0)                    | 4 (10)              | 0/4 (0)                    |
| High fibre diet +/− bran (1)       | 10 (25)             | 5/10 (50)                  |
| Oral laxatives (2)                 | 24 (60)             | 16/24 (67)                 |
| Enemas, PEG or rectal suppositories (3) | 2 (5)          | 0/2 (0)                    |
| Total                              | 40 (100)            | 21/40 (52.5)               |

*Asian consensus on irritable bowel syndrome, †These patients had localized erythema/loss of vascular pattern with proven solitary rectal ulcer syndrome on histopathology, ‡P = 0.030.
BET, balloon expulsion test; PEG, polyethylene glycol.

as applicable. Continuous data were analyzed using Mann-Whitney U test. P-values below 0.05 were considered significant. Data were analyzed by SPSS version 15 (SPSS, Inc., Chicago, IL, USA) and by R, Epicalc and R-studio software (R development core team, Vienna, Austria).

Results

Demographic and Clinical Characteristics of Patients

Patients with SRUS (n = 40) were comparable with HC (n = 19) in age (37 [18-80] vs. 43 [25-72] years, P = 0.300) and gender (26/40 [65%] male vs. 10/19 [53%] male, P = 0.300).

Clinical Characteristics of Patients With Solitary Rectal Ulcer Syndrome

All the 40 patients with SRUS had long standing symptoms (4 [range, 1-20] years). Common symptoms were mucus discharge per rectum (n = 34, 85%), feeling of incomplete evacuation (n = 31, 77%), bleeding per rectum (n = 30, 75%), straining (n = 28, 70%), manual evacuation of stool (n = 27, 68%) and tenesmus (n = 11, 27%). The stool patterns of patients with SRUS are presented in Table 1. They passed 21 (range, 1-56) stools per week. Most patients (36/40 [90%]) had chronic constipation according to the Rome III criteria.

Table 1 summarizes the clinical characteristics of patients with SRUS with and without abnormal BET. Laxative consumption was noticed in 90% of patients. However patients with
Table 2. Comparison of Anorectal Manometry and Balloon Expulsion Test Among Patients With Solitary Rectal Ulcer and Healthy Controls

| Parameters                              | SRUS (n = 40) | HC (n = 19) | P-value\(^a\) |
|-----------------------------------------|--------------|-------------|---------------|
| Sphincter length (cm)\(^b\)            | 2.5 (1-4.5)  | 2.5 (1.5-3.5)| 0.730         |
| Anal resting pressure (mmHg)\(^b\)     | 59.5 (21-106)| 73 (24-95)  | 0.640         |
| High resting pressure (n [%])          | 17 (42)      | 10 (52)     | 0.460\(^e\)  |
| Anal squeeze pressure (mmHg)\(^b\)     | 120.5 (42-248)| 103 (60-195)| 0.200         |
| High squeeze pressure (n [%])          | 8 (20)       | 3 (16)      | 0.690\(^e\)  |
| Anal residual pressure (mmHg)\(^b\)    | 30.5 (2-71)  | 30 (4-68)   | 0.570         |
| Rectal defecation pressure (mmHg)\(^b\)| 58.5 (15-116)| 65 (26-123)| 0.630         |
| Balloon volume at first sensation (mL)\(^b\)| 40 (20-120)| 40 (10-100)| 0.960         |
| High threshold for first sensation (n [%]) | 29 (72)     | 11 (58)     | 0.260\(^e\)  |
| Balloon volume at urge (mL)\(^b\)      | 80 (0-200)   | 80 (20-200) | 0.850         |
| High threshold for urge sensation (n [%]) | 23 (57.5)  | 9 (47)      | 0.460\(^e\)  |
| Balloon volume at maximum tolerance (mL)\(^b\) | 220 (80-400) | 200 (70-400)| 0.460         |
| High threshold for maximum tolerance (n [%]) | 30 (75)      | 13 (68)     | 0.590\(^e\)  |
| Balloon weight at expulsion (g)         | 300 (0-700)  | 100 (0-400) | 0.006         |
| Abnormal BET (n [%])\(^c\)            | 21 (33)      | 5 (26)      | 0.038\(^e\)  |
| Percentage of anal relaxation          | 38.2 (0-96)  | 48 (0-94)   | 0.150         |
| Abnormal anal relaxation\(^d\)         | 14           | 2           | 0.048\(^e\)  |

\(^a\)Mann-Whitney U test, \(^b\)Median (range), \(^c\)Abnormal balloon expulsion test defined as balloon expulsion at weight greater than 200 g, \(^d\)Number of patients with 20% anal relaxation from baseline, \(^e\)Chi-squared test.

SRUS, solitary rectal ulcer syndrome; HC, healthy controls.

abnormal BET more often reported consuming laxative than those without it (21/21 [100%] vs. 15/19 [79%], \(P = 0.030\)). All the other symptoms were comparable between the 2 groups.

**Findings at Proctosigmoidoscopy**

On proctosigmoidoscopy, the ulcerative lesions were solitary in 23 (57%) and multiple in 7 (18%) patients, respectively (Figure A and B). Ten (25%) patients had focal area of hyperemia, loss of vascular pattern, nodularity and polypoid lesions at a location typical of SRU (Table 1). On histopathology, features suggestive of SRU were found in all of them. Ten (25%) patients had associated hemorrhoids.

**Comparison of Anorectal Manometry and Balloon Expulsion Test Among Patients With Solitary Rectal Ulcer and Healthy Control (see Table 2)**

The weight needed to expel the balloon was higher among patients with SRU compared to HC (300 [0-700] g vs. 100 [0-400] g, \(P = 0.006\)). BET more often tended to be abnormal among patients with SRUS compared to HC (21 [33%] vs. 5 [26%], \(P = 0.058\)). Impaired anal relaxation (Figure D) was more frequently detected among patients with SRUS than HC (14/40 [35%] vs. 2/19 [10.5%], \(P = 0.040\)). All other ano-rec-tal manometry parameters were comparable among patients with SRU and HC (Table 2).

**Endoscopic Ultrasonography Parameters Among Patients With Solitary Rectal Ulcer With Normal and Abnormal Balloon Expulsion Test (see Figure)**

Sixteen patients with SRUS underwent anorectal EUS (8 with and other 8 without abnormal BET). IAS was thicker among patients with SRUS with abnormal BET as compared to those without (3.9 [3.4-7.0] mm vs. 2.8 [2.0-4.0] mm, \(P = 0.010\)) (Table 3).

**Defecography in Patients With Solitary Rectal Ulcer Syndrome**

Twenty-two (55%) patients with SRU had abnormal defecography. Anterior rectoceles (n = 8) (Figure C), posterior rectoceles (n = 3), non-relaxing puborectalis (n = 3), prolonged contrast retention (n = 5), rectal intussception (n = 2) and megarectum (n = 1) were the abnormalities detected.
Table 3. Comparison of Patients With Normal and Abnormal Balloon Expulsion Test Among Solitary Rectal Ulcer Syndrome Based on Endoscopic Ultrasound

| Thickness on EUS (mm) | Normal BET (n = 8) | Abnormal BET (n = 8) | P-valuea |
|-----------------------|--------------------|----------------------|----------|
| Internal anal Sphincter | 2.8 (2.0-4.0)      | 3.9 (3.4-7.0)        | 0.010    |
| External anal Sphincter | 5.9 (3.7-7.5)      | 6.4 (4.6-16.0)       | 0.110    |
| Puborectal sling       | 7.2 (4.8-9.1)      | 10.0 (4.7-23.0)      | 0.500    |

EUS, endoscopic ultrasound; BET, balloon expulsion test. Data expressed as mean (range), aMann-Whitney U test.

Discussion

The present study showed that, patients with SRUS (1) more often had chronic constipation by the Rome III criteria, (2) had FED as compared to HC as documented by BET and impaired anal relaxation, (3) more than half of patients with SRU had abnormal defecography, (4) about 40% of the patients with SRU had functional defecation disorders according to the Rome III criteria and (5) those with abnormal BET had thicker IAS than those without.

Pathogenesis of SRUS is largely unknown. Mucosal ischemia was proposed to be one of the mechanisms in the past. A few recent uncontrolled studies on small number of patients suggested a role of FED in the pathogenesis of SRUS. In an uncontrolled study from Netherlands, 3 of 19 patients who underwent defecography were found to have functional defecation disorder. In another uncontrolled observational study from Turkey, 9 of 34 patients with SRUS were found incontinent based on symptoms and had low anal resting and squeeze pressure on ARM. In a recent controlled study, FED was found to be commoner among 11 patients with SRU than 15 controls. Moreover, in this study, biofeedback retraining, which is used to correct FED, led to reduction in bleeding per rectum and healing of SRU. The present study, perhaps, is the largest case-control study showing that FED is associated with SRU.

Another interesting observation in the current study, which is documented perhaps for the first time in the literature, is thickening of IAS among patients with SRU and abnormal BET than those without. This is not entirely unexpected though there is no study in the literature to compare with. However, taking the analogy of achalasia cardia, which is a motility disorder of esophagus, thicker lower esophageal sphincter is associated with poorer esophageal emptying and poorer response to treatment.

Interestingly, a large proportion of patients with SRU had constipation using the Rome III criteria and used laxatives in spite of passing type IV and even types V and VI stool; the latter types of stools are diagnostic of diarrhea according to the recent Asian consensus. Such discordance might be explained by the fact that in the presence of FED, it may be difficult to evacuate even the liquid stool due to functional obstruction of anorectal outlet. This finding, therefore not only supports the importance of functional anorectal obstruction in SRUS but also suggests that use of laxative or fiber supplement may not be very efficient in the management of constipation in patients with SRU and supports the role of biofeedback, which has been found to be useful in the management as reported in a recent study on a small number of patients. This observation also underscores the value of Asian criteria for diagnosis of constipation among patients with FED and SRUS.

The number of patients who reported mucus in their stool, digital evacuation and excessive straining were higher than those reported earlier. However, blood in stool was similar as described previously. Earlier, it has been suggested that rectal mucosal intussusception is a pathognomonic finding in patients with SRUS. In the present study, only 2 (5%) of our patients showed mucosal intussusception and none had rectal prolapse as reported in other studies. Therefore, our study suggests that SRUS is not necessarily associated with rectal intussusception or prolapse.

One-fourth of our patients presented without rectal ulcer, another one-fifth had more than one ulcer and a few patients had rectal polyps. Thus, as described earlier, the term SRUS is a misnomer as ulcer is not always present and may not be solitary. Hemorrhoids were present in one-fourth of the patients, which can be explained by excessive straining during defecation.

We found that a large proportion of patients with SRU had underlying FED and those with FED had thicker IAS. However, whether FED and increased IAS thickness are causes or effects of SRUS is not known. We believe that present study is important as it is the only prospective case-control study with a large sample size, which not only showed association of FED af-
ter detail evaluation but also described for the first time the association of increased in IAS thickness and FED. We believe that further studies may be needed to correlate reversibility of thickness of IAS after biofeedback among those with abnormal BET with SRUS.

In conclusion, FED was more common among patients with SRUS as evidenced by abnormal BET and sphincter relaxation. Those with abnormal BET had thicker internal anal sphincter on EUS than those without.

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