Association between defecation frequency and erectile dysfunction in patients with ulcerative colitis: A cross-sectional study

Shinya Furukawa

shinya.furukawa@gmail.com

Ehime University  https://orcid.org/0000-0002-0041-7688
Teruki Miyake
Osamu Yoshida
Masakazu Hanayama
Shogo Kitahata
Tomoyuki Ninomiya
Sen Yagi
Seiyyu Suzuki
Naozumi Shibata
Katsuhisa Ohashi
Kana Shiraishi
Kazuhiko Tange
Yu Hashimoto
Hideomi Tomida
Yasunori Yamamoto
Eiji Takeshita
Toshio Ikeda
Yoichi Hiasa

Ehime University Graduate School of Medicine  https://orcid.org/0000-0003-4117-339X

Article

**Keywords:** ulcerative colitis, constipation, defecation, erectile dysfunction

**Posted Date:** November 7th, 2023

**DOI:** https://doi.org/10.21203/rs.3.rs-3539729/v1

**License:** ☺️ This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Additional Declarations: There is NO conflict of interest to disclose.

Version of Record: A version of this preprint was published at International Journal of Impotence Research on April 8th, 2024. See the published version at https://doi.org/10.1038/s41443-024-00884-9.
Abstract

The association between ulcerative colitis (UC) and erectile dysfunction (ED) was reported. However, no evidence regarding the association between gastrointestinal symptoms and ED in UC exists, some studies showed the association between gastrointestinal symptoms and ED. The aim of this study is to investigate the association between defecation frequency and ED in 164 patients with UC. The definition of ED was the Sexual Health Inventory for Men score < 12. The defecation frequency was divided into three categories: 1) high (at least two times/day), 2) moderate (once a day, reference), and low (less than one time/day). The definition of constipation was based on the Rome I criteria and/or medication for constipation. The prevalence of ED and constipation was 54.9%, and 10.4%, respectively. The rate of high, moderate, and low defecation frequency was 18.9%, 25.0%, and 56.1%, respectively. High and low frequency defecation was independently and positively associated with ED (High: adjusted OR 4.15, 95% CI 1.36–13.46, and low: adjusted OR 2.77, 95% CI 1.18–6.77). P for quadratic trend, p = 0.007). No association between constipation and ED was found. In Conclusion, in Japanese patients with UC, the U-shaped association between defecation frequency and ED was found.

Introduction

Ulcerative colitis (UC) is one of inflammatory bowel disease (IBD) with repeated remission and relapse, and its etiology is still unknown. Estimated incidence rates of UC remain high in Western countries and are reported to be still increasing in Asian countries [1, 2].

Erectile dysfunction (ED) is defined as a male sexual dysfunction and is the repeated or sustained inability to obtain and/or maintain an erection sufficient for sexual intercourse [3]. Recent meta-analyses have shown that UC is a risk factor for ED [4–6]. However, the reason why the prevalence of ED is higher in UC is not fully understood.

Two previous studies showed the positive association between gastrointestinal symptoms and ED [7, 8]. Irritable bowel syndrome (IBS) and constipation are significantly and positively associated with ED [7, 8]. In patients with UC, frequent bowel movement is a common gastrointestinal symptom [1]. Additionally, the prevalence of constipation is high in UC [9]. While the prevalence of ED in patients with UC is high, no evidence regarding the association between gastrointestinal symptoms and ED in patients with UC exists. We hypothesized that defecation frequency including constipation would be positively associated with the prevalence of ED in UC.

The purpose of this study was to investigate the association between defecation frequency and ED in Japanese patients with UC.

Materials and Methods

Study population
The present study employed a cross-sectional design using baseline data from a prospective cohort study (during the period from 2015 to 2019). 203 male patients with UC who visited Ehime University Hospital, or several affiliated hospitals were enrolled in this study. Inpatients and outpatients diagnosed as UC from mainly endoscopic findings were considered able to complete the questionnaire were candidates for this study. All patients were informed of the study by trained staff and provided written informed consent. All patients in this study were informed about the study by well-trained staff and gave written informed consent. The study protocol was prepared in accordance with the 1964 Declaration of Helsinki and subsequent ethical guidelines and was approved by the Ethics Committee of Ehime University School of Medicine (approval number 1505011). This study is also registered UMIN (000051334).

**Measurements**

A self-administered questionnaire was utilized to collect the information on patients' smoking habits, and alcohol consumption. Body mass index (BMI) was calculated by dividing the participant's weight (kg) by the square of their height (m²). Medical records were also reviewed to obtain information on medication for UC, disease extent, and duration of UC. Certified endoscopists evaluated endoscopic activity by total colonoscopy and reported endoscopic findings and key images. Mucosal healing (MH) is widely considered a goal of treatment in clinical practice and MH (Mayo endoscopic score category 0) was used as the treatment status of UC itself in this study [10]. The assessment methods for Mayo endoscopic score and MH were also described in detail in previous studies of this cohort [11].

**The definition of constipation and defecation frequency**

The information regarding constipation, medication for constipation, and defecation frequency was obtained using self-administered questionnaire. We used the Rome I criteria for investigate the prevalence of constipation [12]. The definition of constipation based on Rome I criteria and/or drug use for constipation.

**The definition of erectile dysfunction (ED)**

The definition of ED in this study was a Sexual Health Inventory for Men (SHIM) score < 12 obtained using a self-administered questionnaire [13].

**Statistical analysis**

The defecation frequency was divided into three categories: 1) high frequency defecation (at least two times/day), 2) moderate frequency defecation (once a day, reference), and low frequency defecation (less than one time/day). Logistic regression analysis was used to estimate crude odds ratios (ORs) and their 95% confidence intervals (CIs) for ED related to the prevalence of constipation and defecation frequency. Adjustments were performed using multiple logistic regression analysis with age, current drinking habits, current smoking habits, BMI, MH and constipation medication use as potential confounders. Trends in association were assessed using logistic regression models assigning consecutive whole numbers to the defecation categories. Linear and quadratic terms were included in the model for testing quadratic trends.
All statistical analyses were performed using the SAS software package version 9.4 (SAS Institute Inc.). All probability values for statistical tests were two-tailed, with \( p < 0.05 \) considered statistically significant.

## Results

### Study characteristics of this cohort.

The clinical characteristics of this study was shown in Table 1. The mean age and SHIM score was 52.1 ± 17.0 and 11.1 ± 8.3. The prevalence of constipation and ED, the rate of medication for constipation, high, moderate, and low frequency defecation was 10.4%, 54.9%, 9.2%, 18.9%, 25.0%, and 56.1%, respectively.
Table 1
Clinical characteristics of 164 study participants

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>52.1 ± 17.0</td>
</tr>
<tr>
<td>Disease extent</td>
<td></td>
</tr>
<tr>
<td>Pancolitis/ left-sided/ proctitis/ others</td>
<td>74/41/44/5</td>
</tr>
<tr>
<td>Duration of UC, year, mean ± SD</td>
<td>7.6 ± 8.0</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>23.24 ± 4.39</td>
</tr>
<tr>
<td>Current smoking (%)</td>
<td>16 (9.8)</td>
</tr>
<tr>
<td>Current drinking (%)</td>
<td>77 (47.0)</td>
</tr>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>5-aminosalicylates (%)</td>
<td>155 (94.5)</td>
</tr>
<tr>
<td>Prednisolone (%)</td>
<td>35 (21.3)</td>
</tr>
<tr>
<td>Thiopurines</td>
<td>24 (14.6)</td>
</tr>
<tr>
<td>TNF-α monoclonal antibody (%)</td>
<td>6 (3.7)</td>
</tr>
<tr>
<td>Mayo Endoscopic Subscore, mean ± SD</td>
<td>1.26 ± 0.91</td>
</tr>
<tr>
<td>Complete mucosal healing (Mayo Endoscopic Subscore &lt; 1) (%)</td>
<td>40 (24.4)</td>
</tr>
<tr>
<td>Constipation</td>
<td>17 (10.4)</td>
</tr>
<tr>
<td>Medication for constipation</td>
<td>15 (9.2)</td>
</tr>
<tr>
<td>Defecation frequency</td>
<td></td>
</tr>
<tr>
<td>High frequency (At least two times/day)</td>
<td>31 (18.9)</td>
</tr>
<tr>
<td>Moderate frequency (One daily)</td>
<td>41 (25.0)</td>
</tr>
<tr>
<td>Low frequency (Less than one time/day)</td>
<td>92 (56.1)</td>
</tr>
<tr>
<td>SHIM score</td>
<td>11.1 ± 8.3</td>
</tr>
<tr>
<td>Erectile dysfunction (SHIM score &lt; 12)</td>
<td>90 (54.9)</td>
</tr>
</tbody>
</table>

BMI, body mass index; UC, ulcerative colitis; SD, standard deviation; TNF, tumor necrosis factor; SHIM, the Sexual Health Inventory for Men; Others: right-sided, segmental colitis and postoperative patients (lack of any preoperative medical records for postoperative patients)

**Association between constipation and ED**
The association between constipation, medication for constipation, and ED is shown in Table 2. In crude analysis, both constipation and medication for constipation was positively associated with ED, respectively (constipation: crude OR 4.36, 95% CI 1.35–19.48, and medication for constipation: crude OR 6.08, 95% CI 1.61–39.73). After adjustment for confounding factors, the association between constipation, medication for constipation and ED was disappeared.

Table 2
Crude and adjusted odds ratios and 95% confidence intervals for the associations between constipation and ED

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence, n/n (%)</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>76/147 (51.7)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>14/17 (82.4)</td>
<td>4.36 (1.35–19.48)</td>
<td>2.54 (0.89–12.38)</td>
</tr>
<tr>
<td>Medication for constipation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>77/149 (51.7)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>13/15 (86.7)</td>
<td>6.08 (1.61–39.73)</td>
<td>3.64 (0.82–26.12)</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; ED, erectile dysfunction

Odds ratios were adjusted for sex, age, body mass index, current drinking, current smoking, and mucosal healing.

Defecation frequency and ED

Table 3 shows the association between defecation frequency and ED. The prevalence of ED in high, moderate, and low frequency defecation was 67.7%, 34.2%, and 59.8%, respectively. In the crude analysis, high and low frequency defecation was positively associated with ED (High: crude OR 4.05, 95% CI 1.54–11.31, and low: crude OR 2.87, 95% CI 1.35–6.31). After adjustment for age, BMI, current smoking, current drinking, and MH (model 1), high and low frequency defecation was independently and positively associated with ED (High: adjusted OR 4.05, 95% CI 1.54–11.31, and low: adjusted OR 2.87, 95% CI 1.35–6.31). P for quadratic trend, p = 0.005). After further adjustment by adding medication for constipation to the confounding factors (model 2), a positive association between high and low frequency defecation and ED was still significant (High: adjusted OR 4.15, 95% CI 1.36–13.46, and low: adjusted OR 2.77, 95% CI 1.18–6.77). P for quadratic trend, p = 0.007).
Table 3
Crude and adjusted odds ratios and 95% confidence intervals for the associations between defecation frequency and ED

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence, ( n/n (%) )</th>
<th>Crude OR (95% CI)</th>
<th>Model 1 Adjusted OR (95% CI)</th>
<th>Model 2 Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Defecation frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High frequency</td>
<td>21/31 (67.7)</td>
<td>4.05 (1.54–11.31)</td>
<td>4.58 (1.53–14.64)</td>
<td>4.15 (1.36–13.46)</td>
</tr>
<tr>
<td>Moderate frequency</td>
<td>14/41 (34.2)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Low frequency</td>
<td>55/91 (59.8)</td>
<td>2.87 (1.35–6.31)</td>
<td>2.86 (1.23–6.93)</td>
<td>2.77 (1.18–6.77)</td>
</tr>
<tr>
<td>( P ) for quadratic trend</td>
<td></td>
<td>0.005</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval; ED, erectile dysfunction

Discussion

This is the first study was to investigate the gastrointestinal symptoms and ED in patients with UC. In this study, both high and low frequency defecation was independently and positively associated with ED. the U-shaped association between defecation frequency and ED was found in patients with UC.

Previous meta-analyses have shown a close association between UC and ED [4–6]. The reason why the UC cause ED is still unclear. A positive association between gastrointestinal symptoms and ED is found in two Asian population-based studies. IBS may have symptoms of constipation, diarrhea, and frequent bowel movements. In a Taiwanese population-based study of 88,040 patients, the incidence of ED in the participants with IBS is significantly higher than those with non-IBS [7]. In a Singapore cross-sectional study of 2276 subjects including 1143 male, the prevalence of constipation is significantly and positively associated with ED [8]. In this study, the low frequency defecation was independently positively associated with ED. However, the prevalence of constipation, and rate of medication for constipation were
positively associated with ED in crude analysis but not adjusted analysis. The discrepancies between previous population-based studies and the present study might be explained at least by mainly sample size and definition of constipation.

UC itself might cause a variety of gastrointestinal symptoms including high frequent bowel movement, diarrhea, mucous-blood stool, and constipation [1, 9]. However, the association between disease activity of UC and ED is still inconsistent. Three studies showed a positive relationship between disease activity and ED in UC [14–16]. On the other hand, other studies have not confirmed a relationship between disease activity and ED [11, 17]. The differences in the definition of disease activity and sample size for each previous studies may lead to inconsistent results.

The mechanisms underlying the U-shaped association between defecations and ED remain unclear. Peripheral neuropathy is frequently seen in patients with UC [18, 19]. Both sexual dysfunction and constipation are well-known early symptoms of neurological disorders such as Parkinson's disease [20]. The association between defecation abnormalities and ED in UC may be one manifestation of neuropathy. The gut microbiota is also associated with UC itself [21], endothelial dysfunction [22], ED [23], and defecations [24]. Abnormalities in the gut microbiota may cause defecation abnormalities concurrent with ED via endothelial dysfunction, subsequent atherosclerosis and UC-related neuropathy. However, further research on gastrointestinal symptoms and sexual function, including ED, is needed.

The study has several limitations. First, this is the cross-sectional study design. Thus, the findings in this study could not establish a causal relationship between defecation frequency and ED. Second, the assessment of ED and defecation frequency was based on self-administered questionnaire. Third, the sample size of this study may be too small to demonstrate an association between constipation and ED. Finally, the study population may be representative of Japanese patients with UC. the prevalence of constipation in the present study was lower than in previous studies of patients with UC, which may be a possible selection bias. However, gender, age and frequency of each class of drug were similar between this study and the Japanese national UC claims-based study [25].

In conclusion, both high and low frequency defecation was independently and positively associated with ED in patients with UC. Further study regarding digestive symptoms and sexual dysfunction is warranted in patients with UC in the future.

Declarations

Acknowledgements

The authors would like to thank Kenichiro Mori, Keitarou Kawasaki, Yuji Mizukami, Satoshi Imamine, Masamoto Torisu, Harumi Yano, Makoto Yano, Masato Murakami, Aki Hasebe, Masumi Hino, and Tomo Kogama.

Authors contributions
Conceptualization: Shinya Furukawa, Yoichi Hiasa, Eiji Takeshita, and Yoshio Ikeda


Formal analysis: Shinya Furukawa

Software: Shinya Furukawa

Supervision: Yoichi Hiasa

Writing: Shinya Furukawa, Teruki Miyake, Osamu Yoshida

All authors have contributed significantly. All the authors have approved the manuscript and agree with submission to your esteemed journal.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

All patients in this study were informed about the study by well-trained staff and gave written informed consent. The study protocol was prepared in accordance with the 1964 Declaration of Helsinki and subsequent ethical guidelines and was approved by the Ethics Committee of Ehime University School of Medicine (approval number 1505011). This study is also registered UMIN (000051334).

Competing Interests

The authors have no conflicts of interest to declare.

References


