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Original Research Article

Risk Factors Associated with Painful Colonoscopy and Prolonged Cecal Intubation Time in Female Patients

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Abstract

Objectives: Few studies have examined risk factors leading to painful colonoscopy and prolonged cecal intubation time in female patients. We aimed to determine the factors associated with painful colonoscopy and prolonged cecal intubation time in female patients.

Methods: This retrospective study analyzed prospectively collected data from a randomized controlled trial with female patients who underwent colonoscopy. Multivariate logistic and linear regression analyses were performed using the following factors that might be associated with painful colonoscopy and prolonged cecal intubation time, respectively: age, body mass index, history of colonoscopy, previous abdominal surgery, routine use of laxatives, inadequate bowel preparation, sigmoid colon diverticulosis, use of a small-caliber colonoscope, and an inexperienced operator.

Results: The study enrolled 219 female patients aged >20 years. Using the receiver operating characteristic curve, painful colonoscopy was defined in cases where the visual analogue scale of overall pain was ≥50 mm. Logistic regression analysis for risk factors associated with painful colonoscopy revealed that sigmoid colon diverticulosis [odds ratio (OR), 2.496; 95% confidence interval (CI), 1.013-5.646; p=0.028] was a risk factor for painful colonoscopy; conversely, the use of a small-caliber colonoscope was a negative factor for painful colonoscopy (OR, 0.436; 95% CI, 0.214-0.889, p=0.022). In linear regression analysis, inadequate bowel preparation was significantly associated with prolonged cecal intubation time (β-coefficient, 3.583; 95% confidence interval, 0.578-6.588; p=0.020).

Conclusions: Female patients with sigmoid colon diverticulosis are more likely to experience severe pain during colonoscopy, and those with inadequate bowel preparation may require more time for cecal intubation.

Keywords

cecal intubation time, colonoscopy, colorectal cancer, pain, woman

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Introduction

Globally, colorectal cancer (CRC) is the third-most diagnosed cancer and the second leading cause of cancer-related death in female patients[1]. Therefore, CRC screening programs are recommended for older female patients in many countries[2]. In Japan, all female individuals aged ≥40 years are offered fecal immunohistochemical tests as part of a CRC screening program, and those with positive findings are referred for colonoscopy. This has led to an increase in the number of colonoscopies performed nationally.

Colonoscopies performed during CRC screening programs

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must be acceptable and tolerable for participants. In particular, the degree of pain that patients experience should be minimal, and completion of cecal intubation should be easy. These are important factors in promoting colonoscopy during the CRC screening programs[3-5]. However, previous studies have reported that female patients experience more pain and longer cecal intubation time during colonoscopy than male patients[6,7]. This is because colonic looping is more frequent in female patients owing to the angulated colon and adhesions following previous gynecological surgery[8-10]. Therefore, female patients often hesitate to attend colonoscopy during CRC screening programs.

Strategies to prevent severe pain and prolonged cecal intubation time during colonoscopy in female patients have been developed and reported in previous works; these include the use of water-exchange intubation techniques[11-13], small-caliber colonoscopes[14-17], sedation[18,19], and modified bowel preparation regimens[20]. However, these strategies also have certain disadvantages, such as longer cecal intubation time, poor manipulation, adverse effects, or higher costs[13,20-23]. Therefore, they should be used only in female patients who have factors that put them at risk of painful colonoscopy and prolonged cecal intubation time. However, to our knowledge, only a few studies have examined the factors associated with painful colonoscopy and prolonged cecal intubation time in female patients. Thus, we aimed to determine these factors using prospectively collected data from a randomized controlled trial (RCT).

Methods

Ethics approval and consent to participate

This study was approved by the institutional review board on May 10, 2021 (approval number: H2021-094). All procedures were performed in accordance with the guidelines of the committee responsible for human experimentation (institutional and national), and the 1964 Helsinki Declaration and its later amendments. Our institutional ethics committee also approved the opt-out method of obtaining consent for the study; accordingly, patients provided informed consent on the institutional website.

Study population

This study was a post-hoc analysis of an RCT that investigated the efficacy of a small-caliber colonoscope in reducing pain during colonoscopy in female patients[17]. The trial was conducted at our institution between October 2013 and November 2017. The study included 220 female patients aged ≥20 years who underwent unsedated colonoscopy. They were randomly assigned in a 1:1 ratio to either undergo the colonoscopy using a small-caliber (PCF-PQ260L; Olympus Medical Systems, Tokyo, Japan) or a standard (CF-Q260AI; Olympus Medical Systems) colonoscope.

Procedure

All study participants underwent bowel preparation with 2 L of polyethylene glycol solution. The endoscopists assessed the quality of bowel preparation based on the extent of the mucosa visible after suctioning the fluid residue; this was performed using the Aronchick Bowel Preparation Scale (excellent, good, fair, poor, or inadequate)[24]. The procedures were performed by eight experienced operators (board-certified fellows of the Japan Gastroenterological Endoscopy Society, each of whom had performed >2,000 colonoscopies) and four inexperienced operators (trainees, each of whom had performed <500 colonoscopies). During the colonoscopy, a 2-mm transparent cap was attached to the tip of the colonoscope.

All patients underwent colonoscopy using air insufflation. Conventional insertion techniques, including loop resolution, position change, and abdominal compression were used if necessary. Cecal intubation time was defined as the time from the intubation of the rectum to the time when the tip of the colonoscope passed to a point proximal to the ileocecal valve so that the base of the cecum was visible. When the colonoscope could not be inserted further, the colonoscopy was deemed unsuccessful and a second colonoscopy was performed using the alternative colonoscope during the same session by the same endoscopists. Withdrawal time was defined as the time taken to withdraw the tip of the colonoscope from the base of the cecum to the anus and included the amount of time required for observation and biopsy of any detected polyps. We examined the polyp pathology by performing a biopsy during the colonoscopy or an endoscopic resection at a later date. Adverse events included post-procedural bleeding and perforation.

Pain scale

Pain during colonoscopy was assessed using a 100-mm visual analogue scale (VAS). Scores of 0 and 100 points indicated no pain and extreme pain, respectively. Before the procedure, the endoscopists or medical assistants explained the VAS scoring system to the patients. After the procedure, the patients were asked to report the overall pain and maximum pain during the colonoscopy using the VAS. In addition, the patient's unacceptance for unsedated colonoscopy was assessed using a questionnaire, with acceptable or unacceptable responses.

Statistical analyses

Continuous variables are expressed as means and standard deviations (SDs), and categorical variables are expressed as numbers and proportions. Based on previous clinical knowledge and our experience[9,25-33], linear or logistic regression analyses were performed using the following factors

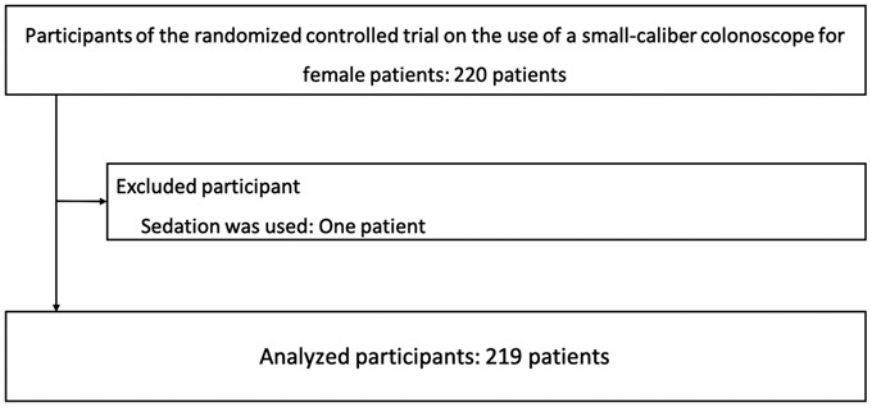

Figure 1. Patient selection process.

Table 1. Baseline Clinical Characteristics (n=219).

Factors	Values
Age, mean (SD), years	62.8 (12.9)
Height, mean (SD), cm	154.2 (6.0)
Weight, mean (SD), kg	52.7 (10.0)
Waist circumference (SD), cm	79.4 (10.8)
Body mass index, n (%)	
Normal (18.5–25.0 kg/m^2)	149 (68.0)
Low (<18.5 kg/m^2)	32 (14.6)
High (>25.0 kg/m^2)	38 (17.4)
Indication for colonoscopy, n (%)	
Positive fecal immunochemical test	75 (34.2)
Screening	45 (20.5)
Polyp surveillance	39 (17.8)
Hematochezia	17 (7.8)
Others	43 (19.6)
Pre-existing factors, n (%)	
History of colonoscopy	112 (51.1)
Previous abdominal surgery	120 (54.8)
Routine use of laxatives	26 (11.9)
Sigmoid colon diverticulosis	34 (15.5)

SD, standard deviation

that might affect pain and cecal intubation time during the colonoscopy: older age, body mass index (BMI) [low (<18.5 kg/m^2) or high (>25.0 kg/m^2)], history of colonoscopies, previous abdominal surgery, routine use of laxatives, inadequate bowel preparation (fair, poor, or inadequate based on the Aronchick Bowel Preparation Scale), sigmoid colon diverticulosis, use of a small-caliber colonoscope, and an inexperienced operator. Factors with statistical significance in univariate analysis were included in the multivariate analysis. A receiver operating characteristic (ROC) curve was constructed using the results of the questionnaire on the patient's unacceptance for unsedated colonoscopy. The cut-off value for the overall pain VAS score used to predict patient intolerability for unsedated colonoscopy was determined at the inflection point of the ROC curve. Consequently, a painful colonoscopy requiring sedation was defined as a case with a VAS score above the cut-off value. All statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA). All tests were two-sided, and a *P*-value <0.05 indicated statistical significance.

Results

Baseline characteristics of enrolled patients

The patient selection process is presented in Figure 1. Of the 220 patients originally enrolled in the RCT, one patient with use of sedation for severe pain during colonoscopy was excluded from the current analysis; thus, the patient cohort included 219 female patients (Figure 1). The baseline characteristics of the enrolled patients are presented in Table 1. The mean (SD) patient age was 62.8 (12.9) years. The major indication for colonoscopy was a positive fecal immunohistochemical test result (34.2%). A total of 112 (51.1%) and 119 (54.8%) patients had previously undergone colonoscopy and abdominal surgery, respectively.

Procedural outcomes

The procedural outcomes are shown in Table 2. The mean (SD) overall and maximum pain scores were 26.0 (24.0) mm and 37.9 (29.7) mm, respectively. The mean (SD) cecal intubation and withdrawal times were 12.3 (8.8) min and 12.3 (5.3) min, respectively. The rate of inadequate bowel preparation was 18.3% (40/219). Colorectal adenomas were detected in 43.4% (95/219) of the patients. The rate of patients' unacceptance for colonoscopy was 6.7% (15/219). No adverse events were observed in any patients.

Cut-off value for painful colonoscopy

As presented in Figure 2, a ROC curve was used to determine the cut-off value to predict intolerability for unsedated colonoscopy. Consequently, the cut-off value was a VAS score of 50 mm with a sensitivity of 73.3% and a specificity

Table 2. Procedural Outcomes of the Patients (n=219).

Factors	Values
Inexperienced operator, n (%)	68 (31.1)
Use of a small-caliber colonoscope, n (%)	109 (49.8)
Procedural pain score, mean (SD), mm*	
Overall pain	26.0 (24.0)
Maximum pain	37.9 (29.7)
Cecal intubation time, mean (SD), min	12.3 (8.8)
Withdrawal time, mean (SD), min	12.3 (5.3)
Total procedure time, mean (SD), min	24.6 (10.1)
Use of abdominal compression, n (%)	128 (58.4)
Change of colonoscope, n (%)	8 (3.7)
Inadequate bowel preparation, n (%) †	40 (18.3)
Adenoma detection, n (%)	95 (43.4)
Patient's unacceptance for unsedated colonoscopy, n (%)	15 (6.7)
Adverse events, n (%)	0 (0.0)

SD, standard deviation

*Procedural pain was evaluated using the visual analog scale.

†Fair, poor, or inadequate based on the Aronchick Bowel Preparation Scale.

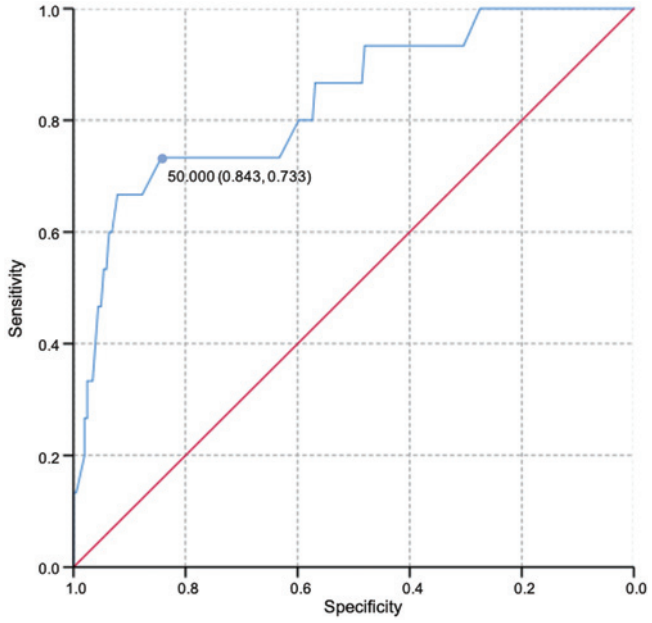

Figure 2. Cut-off value by receiver operating characteristic curve. The cut-off value of the visual analogue scale of overall pain that was associated with painful colonoscopy is 50 mm (sensitivity, 73.3%; specificity, 84.3%; area under the curve, 0.841).

of 84.3. The area under the curve was 83.3. Thus, a painful colonoscopy was defined as a case with a VAS score of overall pain ≥50 mm.

Factors associated with painful colonoscopy

The results of the logistic regression analyses for factors associated with painful colonoscopy are presented in Table 3. The sigmoid colon diverticulosis and the use of a small-caliber colonoscope had a significant difference in the univariate analysis. These factors were also identified as independent factors in multivariate analyses (sigmoid colon diverticulosis: OR, 2.496; 95% CI, 1.103-5.646, p=0.028; use of a small-caliber colonoscope: OR, 0.436; 95% CI, 0.214-0.889, p=0.022).

Factors associated with increased cecal intubation time

The results of the linear regression analyses for factors associated with increased cecal intubation time are presented in Table 4. The inadequate bowel preparation had a significant difference in the univariate analysis. It was also identified as a factor associated with increased cecal intubation time (β-coefficient, 3.583; 95% CI, 0.578-6.588, p=0.020).

Discussion

In the study limited to female patients, we found that sigmoid colon diverticulosis was an independent risk factor for painful colonoscopy, and the use of a small-caliber colonoscope was a negative independent factor for painful colonoscopy. In addition, inadequate bowel preparation was significantly associated with prolonged cecal intubation time.

Many studies have suggested that female sex is a risk factor leading to painful colonoscopy and prolonged cecal intubation time[9,34,35]. Generally, female patients have a more angular sigmoid colon than male patients because of differences in musculoskeletal structure. Moreover, after gynecological surgery, female patients may have adhesions in the pelvis and a freely moving sigmoid colon owing to the larger intra-pelvic space[36-40]. Consequently, these factors may cause severe pain and prolonged cecal intubation time

Table 3. Results of the Logistic Regression Analysis of Factors Responsible for Painful Colonoscopy.

Factors	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Older age, years	0.997 (0.972–1.023)	0.823		
BMI				
Normal (18.5–25.0 kg/m^2)	1			
Low (<18.5 kg/m^2)	1.850 (0.769–4.460)	0.170		
High (>25.0 kg/m^2)	1.260 (0.519–3.060)	0.608		
History of colonoscopy				
Absent	1			
Present	1.001 (0.514–1.950)	0.998		
Previous abdominal surgery				
Absent	1			
Present	1.334 (0.676–2.632)	0.405		
Routine use of laxatives				
Absent	1			
Present	0.718 (0.234–2.204)	0.563		
Inadequate bowel preparation*				
Absent	1			
Present	1.238 (0.539–2.842)	0.614		
Sigmoid colon diverticulosis				
Absent	1		1	
Present	2.710 (1.215–6.044)	0.015	2.496 (1.103–5.646)	0.028
Use of a small-caliber colonoscope				
Absent	1		1	
Present	0.412 (0.204–0.832)	0.013	0.436 (0.214–0.889)	0.022
Inexperienced operator				
Absent	1			
Present	0.829 (0.397–1.735)	0.620		

BMI, body mass index; CI, confidence interval

*Fair, poor, or inadequate based on the Aronchick Bowel Preparation scale.

during colonoscopy. Therefore, female patients often hesitate to undergo colonoscopy during CRC screening programs.

To overcome this issue, several strategies have been reported to reduce the pain and cecal intubation time during colonoscopy, such as the water exchange technique[11-13], use of a small-caliber colonoscope[14-17], sedation[18,19], and modified bowel preparation regimens[20]. However, these strategies also have certain disadvantages. Water-exchange intubation techniques usually have a longer cecal intubation time than those of conventional intubation techniques[12]. A small-caliber colonoscope is less manipulatable than a standard colonoscope, and it is unsuitable for therapeutic colonoscopies. Sedation is associated with various adverse events[21-23]. Modified bowel preparation regimens have a higher cost than those of conventional regimens[20]. Therefore, these strategies should be used only in female patients with risk factors that might lead to painful colonoscopy and prolonged cecal intubation time. However, only a few studies have examined the risk factors associated with painful colonoscopy and prolonged cecal intubation time in female patients.

We examined the factors associated with painful colonoscopy and prolonged cecal intubation time in female patients, based on previous reports and our own experience[9,25-33]. We discovered that the following independent factors play a crucial role: sigmoid colon diverticulosis is associated with painful colonoscopy, and inadequate bowel preparation is associated with prolonged cecal intubation time. Sigmoid colon diverticulosis was reported to be associated with painful colonoscopy[31]. The sigmoid colon diverticulum often becomes infected, causing recurrent diverticulitis. Consequently, this may lead to adhesions in the sigmoid colon, causing severe pain during the passage of a colonoscope. Inadequate bowel preparation has been reported to be associated with prolonged cecal intubation time as the residual stool impairs visualization of the colon[9,30,32]. Therefore, the results of our study are in line with these previous findings.

In this study, the mean cecal intubation time was 12.3 min, which is longer than the corresponding in previous reports (approximately 5-7 min)[14,41]. This difference may be attributed to the following reasons. First, the study par-

Table 4. Results of the Linear Regression Analysis of Factors Leading to Prolonged Cecal Intubation Time.

Factors	Univariate analysis			Multivariate analysis		
	β-coefficient (95% CI)	Standard error	*P*-value	β-coefficient (95% CI)	Standard error	*P*-value
Older age, years	0.020 (-0.069–16.796)	0.046	0.633			
BMI						
Normal (18.5–25.0 kg/m^2)	1					
Low (<18.5 kg/m^2)	0.260 (-3.124–3.644)	1.717	0.880			
High (>25.0 kg/m^2)	2.130 (-1.027–5.286)	2.130	0.185			
History of colonoscopy						
	1					
	0.522 (-1.829–2.873)	1.193	0.662			
Previous abdominal surgery						
	1					
	1.173 (-1.184–3.530)	1.196	0.328			
Routine use of laxatives						
	1					
	0.496 (-3.139–4.130)	1.844	0.788			
Inadequate bowel preparation*						
	1			1		
	3.583 (0.578–6.588)	1.525	0.020	3.583 (0.578–6.588)	1.525	0.020
Sigmoid colon diverticulosis						
	1					
	1.799 (-1.438–5.037)	1.643	0.275			
Use of a small-caliber colonoscope						
	1					
	-1.326 (-3.671–1.018)	1.190	0.266			
Inexperienced operator						
	1					
	0.908 (-1.630–3.446)	1.288	0.481			

BMI, body mass index; CI, confidence interval

* Fair, poor, or inadequate based on the Aronchick Bowel Preparation scale.

ticipants who were limited to female patients affected the cecal intubation time. Interestingly, female sex was reported to be a risk factor for prolonged cecal intubation time[42]. Second, the study participants were limited to patients who underwent unsedated colonoscopy. Especially, previous studies have reported that pain during cecal intubation in unsedated colonoscopy is associated with prolonged cecal intubation time[43,44]. These factors might have led to a longer cecal intubation time than that of previous studies.

Our study had several strengths. First, the original data were prospectively collected for an RCT, which minimized measurement bias. Second, even after full recovery of consciousness, sedated colonoscopy may have caused memory bias in some participants. In contrast, the participants of our study were not given any sedation; therefore, the pain scale could accurately reflect the participant's pain during colonoscopy. Third, this study set a cut-off value for painful colonoscopy and conducted multivariate regression analyses to find the risk factors associated with painful colonoscopy. This result could help clinicians select which patient population might be more suitable to undergo additional interventions, such as sedation or a small-caliber colonoscope.

However, our study had some limitations. First, we could not evaluate the factors that could influence the perception of pain, such as a patient's physical condition and anxiety, which may have increased or decreased the pain threshold. Second, the inadequate bowel preparation rate in this study was 18.3%, higher than those reported in previous studies[45,46]. The reason is considered that more than half of the study participants had a history of abdominal surgery. Previous studies have reported that previous abdominal surgery was an independent risk factor for inadequate bowel preparation[47,48]. The higher rate of inadequate bowel preparation may have affected the study outcomes, which resulted in a bias. Third, this was a single-center study, and the results may not be as generalizable as those obtained from a multicenter study. Similar studies with additional cases and other cohorts will be required to validate our findings.

In conclusion, female patients with sigmoid colon diver-

ticulosis are more likely to experience severe pain during colonoscopy. Moreover, those with inadequate bowel preparation may require more time for cecal intubation. These findings can help guide clinicians to implement targeted strategies to minimize pain and cecal intubation time during colonoscopy for patients with these risk factors.

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Conflicts of Interest

There are no conflicts of interest.

Author Contributions

Yasuhiko Hamada contributed to the study conception and design. Yasuhiko Hamada, Kyosuke Tanaka, Yohei Ikenoyama, Noriyuki Horiki, Junya Tsuboi, Reiko Yamada, and Misaki Nakamura contributed to the data collection. Hayato Nakagawa supervised the study. The first draft of the manuscript was written by Yasuhiko Hamada, and all authors reviewed the subsequent versions of the manuscript. All authors have read and approved the final manuscript.

Approval by Institutional Review Board (IRB)

The study was approved by the ethics committee of Mie University Hospital on May 10, 2021 (approval number H 2021-094).

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