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Risk factors for post-colorectal endoscopic submucosal dissection (ESD) coagulation syndrome: a multicenter, prospective, observational study

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Bibliography
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ABSTRACT

Background and study aims Colorectal cancer (CRC) is one of the most common neoplasms and endoscopic submucosal dissection (ESD) is an effective treatment for early-stage CRC. However, it has been observed that patients undergoing ESD often complain of pain, even if ESD has been successfully performed. Risk factors for such pain still remain unknown. The aim of this study was to explore the risk factors for post-colorectal ESD coagulation syndrome (PECS).

Patients and methods This was a prospective multicenter observational trial (UMIN000016781) conducted in 106 of 223 patients who underwent ESD between March 2015 and April 2016. We investigated age, sex, tumor location, ESD operation time, lesion size, duration of hospitalization, and frequency of PECS. We defined PECS as local abdominal pain (evaluated on a visual analogue scale) in the region corresponding to the site of the ESD that occurred within 4 days of the procedure.

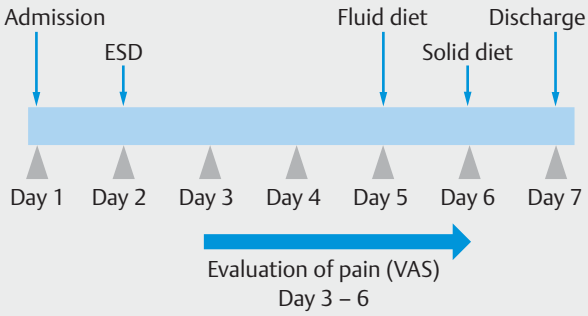
Results PECS occurred in 15/106 (14.2%), and 10 were women ($P=0.01$, OR: 7.74 [1.6–36.4]), 7 had lesions in the cecum ($P<0.001$, OR: 20.6 [3.7–115.2]), and 9 in whom ESD operation time was >90 min ($P=0.002$, OR: 10.3 [2.4–44.6]). Frequency of deviation from the prescribed clinical path was significantly higher (47% [7/15] vs. 2% [2/91], $P<0.001$, OR: 38.9 [6.9–219.6]), and hospital stay was significantly longer in the PECS group.

Conclusions Female gender, location of lesion in the cecum, and ESD operation time >90 minutes were significant risk factors independent of PECS. These findings are important to management of PECS.

Introduction

Incidence of colorectal cancer (CRC) continues to increase worldwide [1, 2] and the importance of early detection and early treatment is growing. Endoscopic submucosal dissection (ESD) has spread rapidly as an effective treatment for early-stage CRC. However, there is a problem because patients frequently complain of pain after ESD even if ESD has been successfully performed. From the viewpoint of patients, pain and distress after treatment are very important issues. With the increased incidence of CRC, the number of colorectal ESD cases can also be expected to continue to increase in the future. Therefore, pain after colorectal ESD is a clinically important issue that needs to be addressed.

Several studies have reported on pain developing after endoscopic procedures. Waye was the first to report the development of pain after polypectomy [3], namely post-polypectomy coagulation syndrome (PPCS). PPCS is thought to be caused by electrical current extending into the muscularis propria and serosa, resulting in a transmural burn at the site of polypectomy [4, 5]. While several studies have also been reported in regard to development of pain after ESD [6 – 8], all of them have been single-center and retrospective, carried out using medical records as reference. All of the relevant information about a patient may not be included in medical records, which could result in a lack of accuracy in studies conducted using information from medical records. To the best of our knowledge, there are no prospective studies that have comprehensively evaluated risk factors for development of pain after colorectal ESD. Precise identification of risk factors can lead to prevention of such pain. Therefore, we performed this prospective observational study for accurate identification of risk factors for post-colorectal ESD coagulation syndrome (PECS).



▶ **Fig. 1** The study protocol and our clinical path for colorectal ESD. We evaluated the pain every morning on post ESD Days 1 to 4 using the Visual Analogue Scale (VAS). Day prior to ESD: Admission to hospital; low-residue diet and 5 mg of oral sodium picosulfate. Day of ESD: 2000 mL of PEG and ESD. Post-ESD Day 1: evaluation of pain (VAS); Post-ESD Day 2: evaluation of pain (VAS); Post-ESD Day 3: evaluation of pain (VAS) and start fluid diet; Post-ESD Day 4: evaluation of pain (VAS) and change to solid diet; Post-ESD Day 5: discharge from hospital.

Patients and methods

Study design and data collection

This study was designed as a prospective, multicenter, consecutive observational study at the Department of Gastroenterology and Hepatology, Yokohama City University Hospital, Yokohama, Japan, and its two affiliate hospitals. We consulted the Department of Anesthesiology and Critical Care, Yokohama City University School of Medicine, Yokohama, Japan, for evaluation of pain. The coordinating office was at Yokohama City University Hospital, with the registration and data collection also conducted at this site. Subject enrolment began in March 2015, and the study was completed in April 2016.

Ethical considerations and registration

The study protocol was in compliance with the Declaration of Helsinki and the Ethics Guidelines for Clinical Research published by the Ministry of Health, Labour and Welfare of Japan. Approval for this study was obtained from the Ethics Committee of Yokohama City University Hospital on 19 January 2015. The protocol and informed consent forms were approved by the institutional ethics committees at each of the participating institutions. The trial protocol was registered in the University Hospital Medical Information Network (UMIN) Clinical Trials Registry as UMIN000016781. Written informed consent for participation in the study was obtained from all participating patients.

ESD procedure

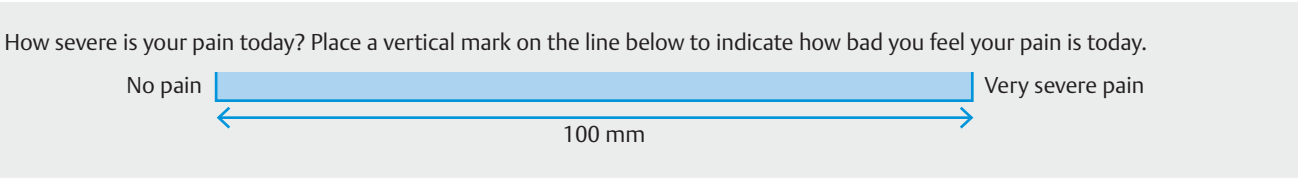
The indication for colorectal ESD was difficulty in resecting the lesion en-bloc by conventional endoscopic mucosal resection (EMR) because: 1) the lesion was larger than 20 mm in diameter; 2) the non-lifting sign was positive after endoscopic injection; and 3) the lesion was judged to not have invaded the muscularis propria. ESD was not performed for lesions that were suspected deep submucosal cancer invasion.

The study protocol and our clinical path for colorectal ESD are presented in ▶ **Fig. 1**. Bowel preparation was initiated the day prior to ESD. Each patient was instructed to consume a low-residue diet and take 5 mg of oral sodium picosulfate on the day before ESD. On the day of ESD, patients received 2000 mL of polyethylene glycol (PEG). If their feces were not sufficiently clear, an additional 1000 to 2000 mL of PEG was given to ensure sufficient bowel cleaning.

All procedures were performed with a standard colonoscope (EVIS CF-Q260DI; Olympus, Tokyo, Japan) or another colonoscope with a water-jet function (EVIS PCF-260JI; Olympus). A transparent hood was attached to the tip of the endoscope in all cases. All procedures were performed with a CO_2 inflation system. Pentazocine (15 mg) was administered routinely at the start of ESD and midazolam was used for sedation, as needed. Cardiorespiratory function was monitored during ESD. The VIO300 D (ERBE Elektromedizin, Tuebingen, Germany) was used as the power source for electrical cutting and coagulation, and tissue dissection was performed with a Dual knife (Olympus). Mucosal incision was carried out using the Dry Cut or Endo Cut current (Effect 2, 30 W) and endoscopic hemostasis was achieved with a coagrasper (Olympus).

Data analysis and definition of PECS

The primary endpoint was identification of risk factors for PECS. We defined PECS as local abdominal pain in the region corresponding to the site of ESD that occurred within 4 days of ESD, in the absence of perforation (▶ **Fig. 1**). We investigated age, sex, tumor location, ESD operation time, lesion size, duration of hospitalization, and frequency of PECS. We excluded patients who: were taking nonsteroidal anti-inflammatory drugs/or any other analgesic drugs, since that could affect pain; were scheduled for multiple colorectal ESDs and/or EMR at the same time, because that may confound precise identification of the cause of PECS; developed perforation during ESD or delayed



▶ **Fig. 2** VAS is a simple descriptive pain scale that consists of a horizontal line, 100 mm in length, 0 mm representing no pain and 100 mm representing the most severe pain. A VAS score in excess of 30 mm (measured from 0 to the point on the line marked by the patient to indicate the severity of his/her pain) was considered as indicative of significant pain.

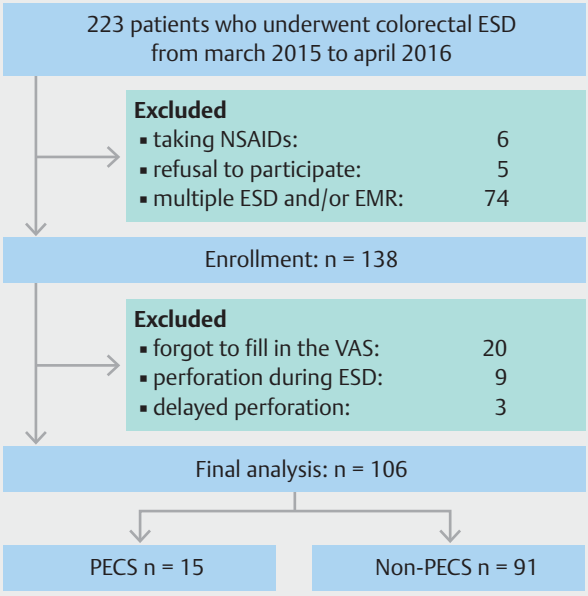
perforation in the peri-procedural period; and had a history of any abdominal surgery. Patients with a history of any symptoms (e. g., diarrhea, abdominal pain), chronic alcohol consumption (> 20 g alcohol/day), or psychiatric disorder were also excluded.

We used a Visual Analogue Scale (VAS) to evaluate presence/absence of pain and also pain severity (▶ **Fig. 2**). The VAS is a simple descriptive pain scale that is often used to measure subjective symptoms that cannot easily be directly measured [9]. VAS is usually a horizontal line, 100 mm in length, with 0 mm representing no pain and 100 mm representing the most severe pain. VAS score is determined by measuring, in mm, the distance from 0 to the point on the line marked by the patient as indicating the severity of his/her pain [10, 11]. Scott et al. [12] reported that VAS is a very sensitive method for evaluating pain, and Collins et al. [13] reported that a baseline VAS score in excess of 30 mm recorded for a patient may be indicative of at least moderate pain. We evaluated presence/absence of pain every morning and also maximum pain severity during the day on post ESD Days 1 to 4 using the VAS for pain (▶ **Fig. 1**). We also evaluated pain severity at other times of the day than in the morning when patients complained of pain to determine maximum severity of pain during the day. We also confirmed presence/absence of pain when patients visited the outpatient clinic 2 weeks after discharge from the hospital.

Blood examination was routinely performed on post-ESD Day 1 (post-admission Day 3), and extra blood examinations were added when patients had any symptoms. After completion of ESD, patients with suspected or known perforation during ESD underwent abdominal computed tomography. Antibiotics were not used routinely but they were used when patients had perforation and we used pentazocine (15 mg) when patients complained of abdominal pain (VAS > 30 mm).

Statistical analysis

Results are presented as means or medians (± standard deviation or range) for quantitative data and as frequencies (percentage) for categorical data. Categorical data were analyzed using the χ^2 test or Fisher's exact test, as appropriate. Data showing normal distribution were compared by the Student's *t*-test, and those showing non-normal distribution were compared by the Mann-Whitney *U* test to assess the statistical significance of differences. $P < 0.05$ was considered as denoting statistical significance. Multivariate analyses were performed using risk factors identified as being significant by univariate analyses. All statistical analyses were carried out using SPSS statistics, version 18 (SPSS, Chicago, Illinois, United States).



▶ **Fig. 3** Study flow of this study. PECS group, n = 15; non-PECS group, n = 91.

Results

Study flow and patient characteristics

A total of 223 patients underwent colorectal ESD at Yokohama City University Hospital and its two affiliate hospitals from March 2015 to April 2016. After excluding 117 patients for various reasons, 106 patients (66 patients from Yokohama City University Hospital, 19 patients from Omori Red Cross Hospital and 21 patients from Hiratsuka City Hospital) were included in the final analysis. A flow diagram of the study is presented in ▶ **Fig. 3**. The major reason for exclusion was multiple ESD and/or EMR scheduled at the same time (n = 74). Patient characteristics are presented in ▶ **Table 1**; mean age ± SD of patients was 71 years (± 9.9). ESD was performed for tumors in the cecum (12 cases), ascending colon (34 cases), transverse colon (15 cases), descending colon (4 cases), sigmoid colon (19 cases) or rectum (22 cases) in 106 patients. Mean lesion size (± SD) was 34.4 mm (± 13.9) and mean ESD operation time (± SD) was 90 min (± 71.3). PECS occurred in 15 of 106 patients (14.2 %), and 14 of 15 PECS occurred on post-ESD Day 1 (post-admission

▶ **Table 1** Characteristics of the patients in this study.

n = 106	
Sex	
▪ Male (%)	67 (63 %)
▪ Female (%)	39 (37 %)
Age (years) mean ± SD (range)	71 ± 9.9 (38 – 90)
Tumor location	
▪ Cecum	12 (11 %)
▪ Ascending colon	34 (32 %)
▪ Transverse colon	15 (14 %)
▪ Descending colon	4 (4 %)
▪ Sigmoid colon	19 (18 %)
▪ Rectum	22 (21 %)
Pentazocine (during ESD) mean ± SD (range) (mg)	
▪ PECS	16 ± 3.8 (15 – 30)
▪ Non-PECS	15.1 ± 1.1 (15 – 22.5)
Midazolam (during ESD) mean ± SD (range) (mg)	
▪ PECS	5.6 ± 3.5 (3 – 16)
▪ Non-PECS	4.4 ± 1.8 (1 – 10)
Specimen size mean ± SD (range) (mm)	34.4 ± 13.9 (17 – 100)
ESD operation time mean ± SD (range) (min)	90 ± 71.3 (10 – 409)

SD, standard deviation; ESD: endoscopic submucosal dissection; PECS, post-colorectal ESD coagulation syndrome.

Day 3) and 1 of the 15 PECS occurred on post-ESD Day 2 (post-admission Day 4). There were no PECS on post-ESD Day 3, 4 (post-admission Day 5, 6).

Risk factors for PECS

PECS occurred in 15 of 106 patients (14.2 %). PECS-related outcomes are presented in ▶ **Table 2**. The mean VAS score (± SD) in the PECS group was 57 mm (± 20.3) while that in the non-PECS group was 4.3 mm (± 7.7). VAS scores in all the subjects are shown in ▶ **Supplementary File 1**. Of the 15 PECS patients, 10 were women ($P = 0.01$, OR [95 % CI]: 3.44 [1.3 – 9.3]) and 7 had lesions in the cecum ($P = 0.0001$, OR [95 % CI]: 6.85 [3.0 – 15.5]). Among patients in whom the resected specimen was > 35 mm in diameter, PECS occurred in 10 ($P = 0.003$, OR [95 % CI]: 4.24 [1.6 – 11.4]), and among patients in whom ESD operation time was > 90 min, PECS occurred in 9 ($P = 0.0005$ OR [95 % CI]: 5.41 [2.1 – 13.6]). There were no significant differences in any of the other variables examined (body mass index, age, fever, white blood cell count [WBC], C-reactive protein [CRP]) between the PECS group and the non-PECS group.

We performed multivariate analysis using the risk factors (female gender, location of lesion in the cecum, resected specimen diameter > 35 mm, ESD operation time > 90 min) that were identified as being significant by univariate analyses. ▶ **Table 3** shows the significant risk factors that were identified by multivariate analysis as being independently associated with development of PECS, namely, female gender ($P = 0.01$, OR [95 % CI]: 7.74 [1.6 – 36.4]), location of the lesion in the cecum ($P < 0.001$, OR [95 % CI]: 20.6 [3.7 – 115.2]) and ESD operation time > 90 min ($P = 0.002$, OR [95 % CI]: 10.3 [2.4 – 44.6]).

The impact on medical care because of PECS is presented in ▶ **Table 4**. The deviation rate from the prescribed clinical path was significantly higher in the PECS group than in the non-PECS group (47 % [7/15] vs. 2 % [2/91], $P < 0.001$, OR: 38.9 [6.9 – 219.6]). The mean fasting period (± SD) in the PECS group was 3.5 (± 1.3) days, while that in the non-PECS group was 2.0 (± 0.1) days. The mean length of hospitalization (± SD) in the PECS group was 8.06 (± 1.6) days, while that in the non-PECS group was 7.01 (± 0.1) days; the length of hospital stay was significantly longer in the PECS group than in the non-PECS group.

Discussion

This is the first prospective multicenter study conducted to identify risk factors for development of pain after colorectal ESD. Previous studies have reported tumor diameter > 40 mm and location in the right-sided colon or in other locations than the rectosigmoid as candidate risk factors for development of coagulation syndrome following ESD [6, 8]. However, all of the studies were retrospective in which information from medical records was used as reference. All relevant medical information about subjects may not be consistently entered in medical records and results of studies based on data entered in medical records may lack accuracy. Therefore, we performed this prospective multicenter observational study to precisely identify risk factors for PECS. We found that significantly higher frequencies of PECS were associated with female gender, location of the lesions in the cecum, and ESD operation times > 90 minutes, thus, these parameters were identified as the risk factors for PECS.

Previous reports in the field of anesthesiology have indicated that women are at a substantially higher risk for many clinical pain conditions, and there is some suggestion that postoperative and procedural pain may be more severe in women than in men [14, 15]. Fillingim et al. [16] reviewed gender differences in incidence of pain summarized for each organ and indicated that abdominal pain, in particular, may be more severe in women [17 – 21]. In addition, Greenspan et al. [22] reported that women have higher sensitivities for pain response to pressure stimulation and electrical stimulation. Colorectal ESD is an abdominal procedure associated with pressure stimulation due to insufflation, and also with electrical stimulation due to electrotomy. Therefore, particular attention may need to be paid to women in surveillance for PECS.

Location of the lesion in the cecum was identified as being a risk factor for PECS. Some researchers have described that the colonic wall is thinner in the right colon than in the left colon [6, 23, 24]. The wall of the cecum is especially easily stretchable and heat after electrocoagulation may extend more easily to the muscularis propria. In addition, in some previous studies of PPCS, most lesions were located in the right colon [23, 25]. Ya-

▶ **Table 2** Risk factors for PECS identified by univariate analysis.

	PECS	non-PECS	*P* value	OR (95 % CI)
Number of subjects	15	91		
Sex			0.01	3.44 (1.3 – 9.3)
▪ Female (%)	10 (67 %)	29 (32 %)		
▪ Male (%)	5 (33 %)	62 (68 %)		
Location of lesion			0.0001	6.85 (3.0—15.5)
▪ Cecum	7 (47 %)	5 (5 %)		
▪ Other colon and rectum	8 (53 %)	86 (95 %)		
Diameter of the resected specimen (mm)			0.003	4.24 (1.6 – 11.4)
▪ >35 mm	10 (67 %)	24 (26 %)		
▪ ≤35 mm	5 (33 %)	67 (74 %)		
ESD operation time (min)			0.0005	5.42 (2.1 – 13.6)
▪ >90 min	9 (60 %)	14 (15 %)		
▪ ≤90 min	6 (40 %)	77 (85 %)		
BMI			0.20	0.90 (0.8 – 1.04)
▪ <25	13 (87 %)	66 (73 %)		
▪ ≥25	2 (13 %)	25 (27 %)		
Age (years)			0.14	1.89 (0.7 – 4.8)
▪ ≥75	8 (53 %)	32 (35 %)		
▪ <75	7 (47 %)	59 (65 %)		
Fever (°C)			0.11	2.69 (0.9 – 7.8)
▪ ≥37.5	3 (20 %)	6 (7 %)		
▪ >37.5	12 (80 %)	85 (93 %)		
WBC count (cells/mL)			0.23	1.61 (0.6 – 4.1)
▪ ≥8000	8 (53 %)	36 (40 %)		
▪ <8000	7 (47 %)	55 (60 %)		
Serum CRP (mg/dL)			0.17	1.90 (0.7 – 5.0)
▪ ≥1.0	5 (33 %)	17 (19 %)		
▪ <1.0	10 (67 %)	74 (81 %)		

PECS, post-colorectal ESD coagulation syndrome; OR, odds ratio; ESD, endoscopic submucosal dissection; CI, confidence interval; BMI, body mass index; WBC, white blood cell; CRP, C-reactive protein.

mashina et al. [8] also reported that location of the lesion in the right colon is one of the risk factors for electrocoagulation syndrome after colorectal ESD. On the other hand, Jung et al. [6] reported location of the lesion in a region other than the rectosigmoid as being a risk factor for development of electrocoagulation syndrome. All of these studies were performed retrospectively and the accuracy of the data in respect to lesion location is subject to question. In the current prospective study, we found that only lesions in the cecum, in terms of lesion location, were associated with a true risk factor for PECS, and our results resolve any past questions about lesion location versus risk of PECS.

ESD operation time >90 minutes also was identified as a risk factor for PECS. Many previous studies [6, 8, 25, 26] have described large tumor size as a risk factor for coagulation syndrome, however, ESD for large tumors generally takes longer. There is the possibility of existence of a correlation between the diameter of the resected specimen and ESD operation time. Therefore, we performed backward selection and eliminated resected specimen diameter >35 mm as a significant variable at the cutoff point of $P<0.20$. Our analysis in the current prospective study identified only ESD operation time >90 minutes as a significant independent risk factor for development of PECS. Insufflation during prolonged ESD may also contribute to

▶ **Table 3** Multivariate analysis conducted to identify significant independent risk factors.

	OR	95 % CI	Multivariate analysis *P* value
Sex			
▪ Female	7.74	1.6 – 36.4	0.01
Location			
▪ Cecum	20.6	3.7 – 115.2	<0.001
ESD operation time			
▪ >90 min	10.3	2.4 – 44.6	0.002

We performed backward selection of four variables that were identified as being statistically significant by univariate analysis (female gender, location of the lesion in the cecum, resected specimen diameter >35 mm, ESD operation time >90 min); resected specimen diameter >35 mm was eliminated as a significant variable at the cutoff point of $P<0.20$.

risk of development of PECS. Lesion size is a factor over which endoscopists have no control, however, ESD operation time may be shortened with improved endoscopist skill [27]. Therefore, it is important for endoscopists to attempt to improve their skill in performing ESD.

In this study, there were no significant differences in WBC count, height/frequency of fever or serum CRP levels between the PECS group and non-PECS group. Yamashina et al. [8] reported that inflammatory response was related to the coagulation syndrome, however, they defined coagulation syndrome as abdominal tenderness with fever or inflammatory response (WBC count >10 000 cells/μL or serum CRP >0.5). It is nothing special because their definition of coagulation syndrome contained inflammatory response. However, it is unknown whether inflammatory response is the cause of pain that develops after ESD. We evaluated pain after ESD using VAS, and our study found no significant association between inflammatory response and development of PECS in actuality. Presence or absence of pain is more clinically significant than presence or absence of inflammatory response.

The deviation rate from the prescribed clinical path was significantly higher in the PECS group than in the non-PECS group, and the mean length of hospitalization was also significantly higher in the PECS group. While distress associated with PECS is an important issue from the viewpoint of patients, prevention/control of PECS is also important from the viewpoint of reducing hospital stays and medical expenses.

Our study had some limitations. First, our telling the patients before ESD that "there is the possibility that pain appears after ESD" may have influenced the patients' reports of pain after ESD. However, it was necessary to provide sufficient explanation to patients to enable them to fill in the VAS with a full understanding of the significance of this research. In our explanations to patients, we consciously paid attention to not giving patients the willies and we made every attempt to minimize the introduction of bias while providing clear information. In addition, we defined VAS >30 mm as the threshold indicating significant pain to exclude pain related to anxiety and mental stress. Therefore, we believe that the influence of anxiety and mental stress on reporting of pain was minimal. Second, because we sometimes used additional pentazocine for analgesia, as necessary during ESD, that could have influenced incidence of PECS. However, it may be ethically unacceptable not to use analgesia for patients complaining of pain. In addition, we administered pentazocine (15 mg) routinely at the start of ESD to align the conditions as much as possible, and pentazocine has a short duration of activity (about 3 – 4 hours). We evaluated pain the morning after ESD (after about 13 – 15 hours). Therefore, pentazocine injection would have had little effect on incidence of PECS. Third, because we did not perform computed tomography (CT) in all patients undergoing ESD, there is a possibility that those with microperforation were included. However, it is not entirely optimal to carry out CT in all patients undergoing ESD, and our main aim was to identify risk factors for PECS in patients without obvious perforation during ESD, regardless of presence or absence of microperforation. Even if the PECS group included some microperforation cases, it had no significant effect on the conclusion of this study. In addition, if the PECS group included a significant number of microperforation cases, inflammatory responses (fever, WBC count, serum CRP) would have been extracted as significant risk factors for PECS. However, we found no relationship between development of PECS and inflammatory responses, suggesting that it is unlikely

▶ **Table 4** Impact on medical care cause of PECS.

	PECS	non-PECS
Fasting period (mean ± SD) (range) (days)	3.5 ± 1.3 (2 – 5)	2 ± 0.1 (2 – 3)
Pentazocine (post-ESD Days 1 – 4) mean ± SD (range) (mg)	5 ± 7.3 (0 – 15)	0.3 ± 2.2 (0 – 15)
Length of hospital stay in the PECS group vs. non-PECS group (days) mean ± SD (range)	8.06 ± 1.6 (7 – 12)	7.01 ± 0.1 (7 – 8)
Deviation rate from the clinical path		
▪ Deviation	7 (47 %)	2 (2 %)
▪ Compliance	8 (53 %)	89 (98 %)

PECS, post-colorectal ESD coagulation syndrome; SD, standard deviation; ESD, endoscopic submucosal dissection.

that a significant number of patients with microperforation were included in the PECS group.

Conclusion

In conclusion, our results indicate that female gender, lesion location in the cecum, and ESD operation time > 90 minutes were significant independent risk factors for PECS. Duration of hospitalization was extended in the PECS group. Thus, PECS is a clinically significant condition and it is important to develop effective methods for prevention/control of it.

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Competing interests

None

References

[1] Torre LA, Bray F, Siegel RL et al. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65: 87 – 108

[2] Anderson WF, Umar A, Brawley OW. Colorectal carcinoma in black and white race. Cancer Metastasis Rev 2003; 22: 67 – 82

[3] Waye JD. The postpolypectomy coagulation syndrome. Gastrointest Endosc 1981; 27: 184

[4] Christie JP, Marrazzo J. "Mini-perforation" of the colon-not all postpolypectomy perforations require laparotomy. Dis. Colon Rectum 1991; 34: 132 – 135

[5] Waye JD, Lewis BS, Yessayan S. Colonoscopy: a prospective report of complications. J Clin Gastroenterol 1992; 15: 347 – 351

[6] Jung D, Youn YH, Jahng J et al. Risk of electrocoagulation syndrome after endoscopic submucosal dissection in the colon and rectum. Endoscopy 2013; 45: 714 – 717

[7] Hong JM, Kim HJ, Lee YS et al. Prevalence and clinical features of coagulation syndrome after endoscopic submucosal dissection for colorectal neoplasms. Dig Dis Sci 2015; 60: 211 – 216

[8] Yamashina T, Takeuchi Y, Uedo N et al. Features of electrocoagulation syndrome after endoscopic submucosal dissection for colorectal neoplasm. J Gastroenterol Hepatol 2016; 31: 615 – 620

[9] Keel KD. The pain chart. Lancet 1948; 2: 6 – 8

[10] Huskisson EC. Measurement of pain. Lancet 1974; 2: 1127 – 1131

[11] Huskisson EC. Visual analogue scales. In: Merzack R ed. Pain measurement and assessment. New York: Raven Press; 1983: 33 – 37

[12] Scott J, Huskisson EC. Graphic representation of pain. Pain 1976; 2: 175 – 184

[13] Collins SL, Moore RA, McQuay HJ. The visual analogue pain intensity scale: what is moderate pain in millimeters? Pain 1997; 72: 95 – 97

[14] Verbrugge LM. Gender and health: an update on hypotheses and evidence. J Health Soc Behav 1985; 26: 156 – 182

[15] Ruau D, Liu LY, Clark JD et al. Sex differences in reported pain across 11,000 patients captured in electronic medical records. J Pain 2012; 13: 228 – 234

[16] Fillingim RB, King CD, Ribeiro-Dasilva MC et al. Sex, gender, and pain: a review of recent clinical and experimental findings. J Pain 2009; 10: 447 – 485

[17] Unruh AM. Gender variations in clinical pain experience. Pain 1996; 65: 123 – 167

[18] Picavet HS, Hazes JM. Prevalence of self reported musculoskeletal diseases is high. Ann Rheum Dis 2003; 62: 644 – 650

[19] Gerdle B, Bjork J, Coster L et al. Prevalence of widespread pain and associations with work status: A population study. BMC Musculoskel Disord 2008; 9: 102

[20] Bassols A, Bosch F, Campillo M et al. An epidemiological comparison of pain complaints in the general population of Catalonia. Pain 1999; 83: 9 – 16

[21] Hardt J, Jacobsen C, Goldberg J et al. Prevalence of chronic pain in a representative sample in the United States. Pain Med 2008; 9: 802 – 812

[22] Greenspan JD, Craft RM, LeReesche L et al. Studying sex and gender differences in pain and analgesia: a consensus report. Pain 2007; 132: S26 – S45

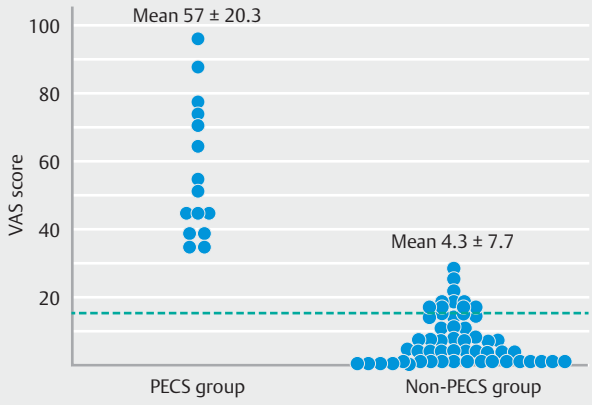
[23] Choo WK, Subhani J. Complication rates of colonic polypectomy in relation to polyp characteristics and techniques: a district hospital experience. J Interv Gastroenterol 2012; 2: 8 – 11

[24] Wong SK, Ho YH, Leong AP et al. Clinical behavior of complicated right-sided and left-sided diverticulosis. Dis. Colon Rectum 1997; 40: 344 – 348

[25] Cha JM, Lim KS, Lee SH et al. Clinical outcomes and risk factors of post-polypectomy coagulation syndrome: a multicenter, retrospective, case-control study. Endoscopy 2013; 45: 202 – 207

[26] Lee H, Cheoi KS, Chung H et al. Clinical features and predictive factors of coagulation syndrome after endoscopic submucosal dissection for early gastric neoplasm. Gastric Cancer 2012; 15: 83 – 90

[27] Ohata K, Nonaka K, Misumi Y et al. Usefulness of training using animal models for colorectal endoscopic submucosal dissection: is experience performing gastric ESD really needed? Endosc Int Open 2016; 4: E333 – E339



▶ Supplementary File 1.