ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2021 October 14; 27(38): 6348-6514

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 27 Number 38 October 14, 2021

EDITORIAL

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Basic Study

Retrospective Cohort Study

Retrospective Study

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Veerapol Kukongviriyapan, PhD, Professor, Department of Pharmacology, Faculty of Medicine, Khon Kaen University, 123 Moo 16, Mittraphap Road, Muang District, Khon Kaen 40002, Thailand. veerapol@kku.ac.th

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Report® cites the 2020 impact factor (IF) for *WJG* as 5.742; Journal Citation Indicator: 0.79; IF without journal self cites: 5.590; 5-year IF: 5.044; Ranking: 28 among 92 journals in gastroenterology and hepatology; and Quartile category: Q2. The *WJG*'s CiteScore for 2020 is 6.9 and Scopus CiteScore rank 2020: Gastroenterology is 19/136.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Ji-Hong Liu*; **Production Department Director:** *Yu-Jie Ma*; **Editorial Office Director:** *Ze-Mao Gong*.

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Andrzej S Tarnawski, Subrata Ghosh

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/1007-9327/editorialboard.htm

PUBLICATION DATE
October 14, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2021 October 14; 27(38): 6442-6452

DOI: 10.3748/wjg.v27.i38.6442

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Retrospective Cohort Study

High total Joule heat increases the risk of post-endoscopic submucosal dissection electrocoagulation syndrome after colorectal endoscopic submucosal dissection

Masanori Ochi, Ryosuke Kawagoe, Toshiro Kamoshida, Yukako Hamano, Haruka Ohkawara, Atsushi Ohkawara, Nobushige Kakinoki, Yuji Yamaguchi, Shinji Hirai, Akinori Yanaka, Kiichiro Tsuchiya

ORCID number: Masanori Ochi 0000-0003-0850-6076; Ryosuke Kawagoe 0000-0001-5283-2384; Toshiro Kamoshida 0000-0003-4930-1018; Yukako Hamano 0000-0003-3491-310X; Haruka Ohkawara 0000-0001-8427-5826; Atsushi Ohkawara 0000-0003-1764-565X; Nobushige Kakinoki 0000-0002-1522-2226; Yuji Yamaguchi 0000-0002-4084-0827; Shinji Hirai 0000-0001-7141-0240; Akinori Yanaka 0000-0001-7967-5665; Kiichiro Tsuchiya 0000-0002-1977-8707.

Author contributions: Ochi M, Kawagoe R, Kamoshida T, Hamano Y, Ohkawara A, Ohkawara H, Kakinoki N, Yamaguchi Y, Hirai S, Yanaka A and Tsuchiya K contributed equally to this work; Ochi M and Kawagoe R collected and analyzed the data; Ochi M and Kawagoe R drafted the manuscript; Ochi M, Kawagoe R and Kamoshida T designed and supervised the study; Hamano Y, Ohkawara A, Ohkawara H, Kakinoki N, Yamaguchi Y, Hirai S, Yanaka A and Tsuchiya K offered technical or material support; all authors have read and approved the final version to be published.

Institutional review board

Masanori Ochi, Toshiro Kamoshida, Yukako Hamano, Haruka Ohkawara, Atsushi Ohkawara, Nobushige Kakinoki, Yuji Yamaguchi, Shinji Hirai, Department of Gastroenterology, Hitachi General Hospital, Hitachi City 317-0077, Ibaraki, Japan

Ryosuke Kawagoe, Akinori Yanaka, Kiichiro Tsuchiya, Department of Gastroenterology, Faculty of Medicine, University of Tsukuba, Tsukuba 305-8576, Ibaraki, Japan

Corresponding author: Masanori Ochi, MD, Doctor, Department of Gastroenterology, Hitachi General Hospital, 2-1-1, Jonancho, Hitachi City, Hitachi City 317-0077, Ibaraki, Japan.
maochi-tei@umin.ac.jp

Abstract

BACKGROUND

We hypothesized that thermal damage accumulation during endoscopic submucosal dissection (ESD) causes the pathogenesis of post-ESD electrocoagulation syndrome (PECS).

AIM

To determine the association between Joule heat and the onset of PECS.

METHODS

We performed a retrospective cohort study in patients who underwent colorectal ESD from May 2013 to March 2021 in Japan. We developed a novel device that measures swift coagulation time with a sensor adjacent to the electrosurgical coagulation unit foot switch, which enabled us to calculate total Joule heat. PECS was defined as localized abdominal pain (visual analogue scale ≥ 30 mm during hospitalization or increased by ≥ 20 mm from the baseline) and fever (temperature ≥ 37.5 degrees or white blood cell count ≥ 10000 μ/L). Patients exposed to more or less than the median Joule heat value were assigned to the high and low Joule heat groups, respectively. Statistical analyses included Mann-Whitney U and chi-square tests and logistic regression and receiver operating characteristic curve (ROC) analyses.

RESULTS

We evaluated 151 patients. The PECS incidence was 10.6% (16/151 cases), and all

patients were followed conservatively and discharged without severe complications. In multivariate analysis, high Joule heat was an independent PECS risk factor. The area under the ROC curve showing the correlation between PECS and total Joule heat was high [0.788 (95% confidence interval: 0.666-0.909)].

CONCLUSION

Joule heat accumulation in the gastrointestinal wall is involved in the onset of PECS. ESD-related thermal damage to the peeled mucosal surface is probably a major component of the mechanism underlying PECS.

Key Words: Post-endoscopic submucosal dissection electrocoagulation syndrome; Joule heat; Colorectal endoscopic submucosal dissection; Colorectal neoplasms; Electrocoagulation; Gastrointestinal tract

Core Tip: We investigated the association between Joule heat and the onset of post-endoscopic submucosal dissection electrocoagulation syndrome (PECS), using originally developed a device to measure swift coagulation time with a sensor adjacent to the electrosurgical coagulation unit foot switch which enabled us to calculate total Joule heat. High Joule heat was an independent PECS risk factor. Moreover, the area under the operating characteristic curve showing the correlation between PECS and total Joule heat was high. Joule heat accumulation is involved in the onset of PECS. endoscopic submucosal dissection-related thermal damage of the peeled mucosal surface is probably a major component of the mechanism underlying PECS.

Citation: Ochi M, Kawagoe R, Kamoshida T, Hamano Y, Ohkawara H, Ohkawara A, Kakinoki N, Yamaguchi Y, Hirai S, Yanaka A, Tsuchiya K. High total Joule heat increases the risk of post-endoscopic submucosal dissection electrocoagulation syndrome after colorectal endoscopic submucosal dissection. *World J Gastroenterol* 2021; 27(38): 6442-6452
URL: https://www.wjgnet.com/1007-9327/full/v27/i38/6442.htm
DOI: https://dx.doi.org/10.3748/wjg.v27.i38.6442

INTRODUCTION

Colorectal endoscopic submucosal dissection (ESD), a minimally invasive operation, is the best endoscopic procedure for *en bloc* resection of superficial colorectal tumors[1-4]. However, ESD is associated with severe complications, with rates of perforation and bleeding of 2% to 14% and 0.7% to 3.1%, respectively[4-10]. Post-ESD electrocoagulation syndrome (PECS) is another notable adverse event that can occur after colorectal ESD. The incidence of PECS is 9% to 40%, although most cases improve with conservative therapy[11-15]. In addition, PECS sometimes manifests as a delayed perforation. Therefore, physicians require clinically useful PECS predictors to identify patients who are at risk[12,16].

Currently, two main hypotheses explain the mechanism underlying PECS. One suggests that ESD exposes the mucosa, which is then infected by intestinal bacteria, resulting in inflammation[13,17]. The other proposes that the peeled mucosal surface is inflamed by thermal damage during ESD[13,18]. Interestingly, a clipping closure method performed to prevent intestinal bacteria from infecting the exposed mucosa did not reduce the onset of PECS[19]. In contrast, few studies have examined the impact of thermal damage during ESD on the onset of PECS.

We have often encountered patients with PECS who underwent a lengthy colorectal ESD, and previous studies of PECS risk factors implicated prolonged ESD procedures [20,21]. We hypothesized that electrocoagulation is associated with Joule heat capable of causing thermal damage to the gastrointestinal wall during long ESD operations. Therefore, we aimed to determine the association between Joule heat and the onset of PECS.

statement: The Hitachi General Hospital Institutional Review Board approved this study (2019-97, 2020-1), and it was performed according to the ethical guidelines of the 1964 Declaration of Helsinki and its later amendments.

Informed consent statement: Informed consent was obtained using an opt-out option on the Hitachi General Hospital's website (see institution website uniform resource locators: http://www.hitachi.co.jp/hospital/hitachi/infor/opto-out/index.html).

Conflict-of-interest statement: All the authors have no conflict of interest related to the manuscript.

Data sharing statement: The original anonymous dataset is available on request from the corresponding author at maochi-tei@umin.ac.jp.

STROBE statement: The authors have read the STROBE Statement - checklist of items, and the manuscript was prepared and revised according to the STROBE Statement -checklist of items.

Manuscript source: Unsolicited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: Japan

Peer-review report's scientific quality classification

Grade A (Excellent): 0

Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: May 24, 2021
Peer-review started: May 24, 2021
First decision: June 22, 2021
Revised: July 17, 2021
Accepted: September 10, 2021
Article in press: September 10, 2021
Published online: October 14, 2021

P-Reviewer: Li YY
S-Editor: Liu M
L-Editor: A
P-Editor: Yuan YY

MATERIALS AND METHODS

Study design and patient selection

We performed a retrospective study in patients who underwent colorectal ESD at Hitachi General Hospital in Japan from May 2013 to March 2021. Case selection was according to the indications for colorectal ESD established by the Japan Gastroenterological Endoscopy Society guidelines[22]. Therefore, our inclusion criteria were as follows: (1) Laterally spreading tumors of the non-granular type with the Vi-type pit pattern, carcinomas with shallow T1 submucosal (SM) invasion, large depressed-type tumors, and large protruded-type tumors that are difficult to remove en bloc by endoscopic mucosal resection; and (2) Mucosal tumors with SM fibrosis. Patients with multiple colorectal neoplasms or apparent deeply invasive T1 SM carcinoma were excluded. R0 resection was defined as no cancer cells seen microscopically at the primary tumor site. We converted the swift-coagulation mode time, measured by an electrosurgical-coagulation unit with a high-frequency generator (VIO 300D, ERBE Co. Ltd., Tubingen, Germany), to Joule heat.

The Hitachi General Hospital Institutional Review Board approved the study (No. 2019-97, 2020-1), and our research was performed according to the ethical guidelines of the 1964 Declaration of Helsinki and its later amendments. The study is registered on the University Hospital Medical Information Network (ID: UMIN000038704, UMIN 000041580). Although our ethics committee waived the requirement for informed consent from each patient because we used anonymized data, we obtained informed consent using an opt-out option on our facility's website (uniform resource locator below).

PECS definition

PECS was defined as localized abdominal pain and fever without apparent perforation after colorectal ESD. We used a visual analog scale (VAS) to evaluate localized abdominal pain. Nurses who were not research participants administered the VAS. The pain criteria were defined as a score ≥ 30 mm from the postoperative day (POD) 1 to discharge or increased by ≥ 20 mm from the hospital admission VAS score. Our fever criteria were body temperature ≥ 37.5 degrees or white blood cell count ≥ 10000 μ/L from POD 1 to discharge.

Colorectal ESD procedures

All patients underwent bowel preparation (polyethylene glycol, 2 L) before colorectal ESD. Then, the patients were sedated in the endoscopy room using intravenous injections of pentazocine (15-30 mg/kg body weight). We added midazolam (1-3 mg/session) if pentazocine was insufficient for sedation. Electrocardiogram monitoring was performed in each case. The procedures were performed by 10 endoscopists (one expert colorectal endoscopic surgeon and 9 less experienced colorectal endoscopic surgeons). An expert was defined as an endoscopist who performed more than 40 colorectal ESDs[23]. We used a water-jet system colonoscope (PCF-Q260JI, Olympus Corporation, Tokyo, Japan) with a transparent hood (DH-29CR for scope tip, Fujifilm, Tokyo, Japan) attached to the scope tip. Marking, mucosal incision, and mucosal detachment were performed with a dual knife (KD-655Q, Olympus Corporation). We injected 0.4% sodium hyaluronate acid diluted in physiological saline into the SM layer directly below the lesion before mucosal detachment. A coagrasper (FD-411QR, Olympus Corporation) and an endoscopic clip (HX-610-090, Olympus Corporation) were used to obtain hemostasis.

Calculating Joule heat

We used the electrosurgical-coagulation unit to detach the lesion's colorectal mucosa. We changed the setting mode according to the procedure step and used dry-cut, swift-coagulation, and soft-coagulation modes. We calculated the power applied using the diagram in the manufacturer's technical manual that shows the relationship between resistance (Ω) and power (W) in the swift-coagulation mode (Supplementary material). As human internal resistance is 1000-1600 Ω[24], the lesion resistance was defined as 1300 Ω. Thus, lesions are detached while the electrosurgical-coagulation unit automatically adjusts the power output. However, this automatic power adjustment is difficult to monitor.

The curve describing the relationship between power (vertical axis) and resistance (horizontal axis) in the manufacturer's technical diagram (we used effect 4 in our study) showed that the power corresponding to 1300 Ω is 50 W (Supplementary material). Therefore, we obtained the formula: power consumption (J) = power (W) ×

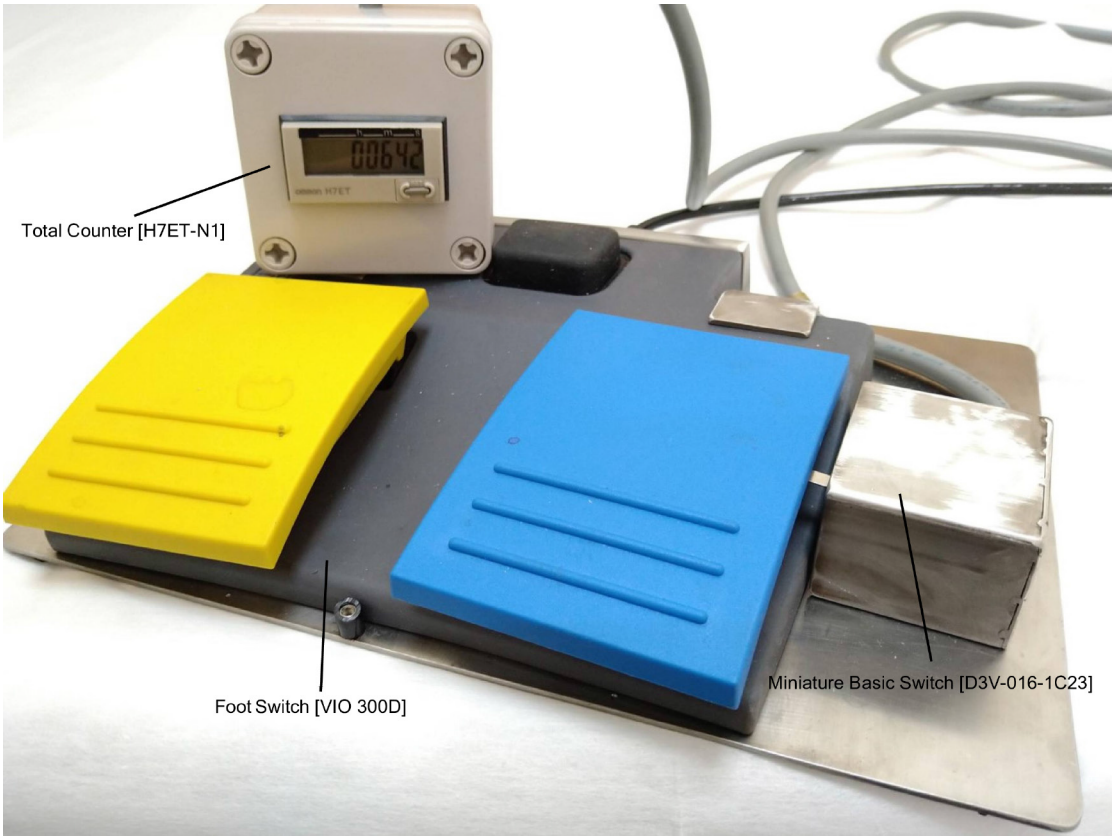

Figure 1 A novel device for measuring the swift-coagulation mode time with a sensor adjacent to the foot switch of the electrosurgical coagulation unit.

time (s) from the relationship between power and power consumption. We used this formula to calculate the total Joule heat applied to the lesion.

We developed a novel device to measure the swift coagulation time with a sensor [Miniature Basic Switch (D3V-016-1C23), OMRON Corporation, Kyoto, Japan] adjacent to the foot switch of the electrosurgical coagulation unit (Figure 1). This sensor was activated when the operator stepped down on the foot switch, and the swift-coagulation mode time was recorded by a counter [Total Counter (H7ET-N1), OMRON Corporation]. In cases where the swift-coagulation time was not measured, we retrospectively calculated the time using the data (swift-coagulation mode time/procedure time: Mean 3%) obtained from the measured cases. Patients exposed to more or less than the median Joule heat value (8460 J) were assigned to the high and low Joule heat groups, respectively.

Post-ESD hospitalization

In all patients, on POD 1, the vital signs and a blood sample were examined to check for bleeding, the pain VAS was administered, and radiography was performed to check for free air. We considered a fever, localized abdominal pain, or increased C-reactive protein suspicious for delayed perforation associated with PECS. If the pain or fever criteria were satisfied, we performed computed tomography. In the absence of adverse findings, patients resumed eating, starting with dinner on POD 1. If no fever, localized abdominal pain, or bleeding occurred after eating resumed, patients were discharged on POD 6.

Statistical analysis

We analyzed continuous and categorical variables using Mann-Whitney U and chi-square tests, respectively. In our multivariate analysis, we performed logistic regression analyses using important factors identified by univariate analysis. We determined the cutoff of the total Joule heat value that predicted the onset of PECS using receiver operating characteristic (ROC) curve analysis. A P value less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 26, IBM Corp., Armonk, NY, United States). The statistical methods of this study were reviewed by Masanori Ochi from the Department of

Gastroenterology, Hitachi General Hospital, Japan.

RESULTS

Baseline characteristics

Of 170 patients admitted for colorectal ESD, 19 met the exclusion criteria (multiple lesions, *n* = 6; post-ESD infection, *n* = 2; perforation during ESD, *n* = 7; ESD discontinuation, *n* = 4) (Figure 2). We analyzed the remaining 151 patients [mean age, 67.3 years (range 39-92); male, 62.3%]. Tumors occurred in the right colon (*n* = 59, 39.1%), left colon (*n* = 41, 27.2%), and rectum (*n* = 51, 33.8%); R0 and *en bloc* resections were achieved in 115 patients (76.2%) and 135 patients (89.4%), respectively; and PECS occurred in 16 patients (10.6 %) (Table 1).

Primary outcome

The high (*n* = 76) and low (*n* = 75) Joule heat groups showed no statistically significant difference in sex; tumor morphology, location, or depth of pathological invasion; R0 resection rate; or incidence of SM fibrosis (Table 2). Univariate analyses revealed that patient age was significantly greater, and the PECS incidence was significantly higher in the high Joule group than in the low Joule group; the specimen size was also significantly larger in the high Joule group. Compared to the low Joule heat group, the high Joule heat group included more patients who had undergone ESD performed by a trainee, and the difference was significant. In addition, the R0 resection rate was significantly higher in the low Joule group. Multivariate analysis showed that the R0 resection rate [odds ratio (OR), 3.27; 95% confidence interval (CI): 1.26-8.45; $P = 0.01$] and PECS incidence (OR, 4.83; 95%CI: 1.08-21.50; $P = 0.03$) were significantly higher and the specimen size (OR, 1.07; 95%CI: 1.03-1.11; $P < 0.01$) and number of ESD procedures performed by a trainee (OR, 5.30; 95%CI: 2.32-12.10; $P < 0.01$) were significantly larger in the high Joule heat group than in the low Joule heat group (Table 3).

PECS and Joule heat correlation analysis

The area under the ROC curve showing the correlation between PECS and total Joule heat was 0.788 (95%CI: 0.666-0.909), and the PECS onset cutoff value was 15390 J (sensitivity, 0.625; specificity, 0.822) (Figure 3).

DISCUSSION

To our knowledge, this study, performed using our novel device, is the first to indicate high total Joule heat exposure during colorectal ESD as a PECS risk factor. Additionally, PECS and Joule heat were highly correlated, and the Joule heat cutoff value where PECS occurred was 15390 J.

PECS is a state of temporary inflammation resulting from transmission of electrocoagulation heat to the resection site muscle layer and serous membrane during endoscopic therapy[18,25,26]. Previously reported PECS risk factors include tumor location[11,13,20,27], SM fibrosis[27], long procedure time[20,21], and specimen diameter[11,13]. Long procedures lead to the occurrence of PECS due to increased electrical current load on the gastrointestinal wall[11]. Additionally, ischemic changes occur in the gastrointestinal wall due to excessive current during incision, dissection, and hemostasis[28]. These reports suggest that Joule heat of the peeled mucosal surface is associated with the occurrence of PECS.

A study of lengthy procedures (mean, 90 min) demonstrated that long procedure time is a PECS risk factor[20]. However, several studies that did not include long procedure time as a PECS risk factor showed that the procedures were short (range, 52-67 min)[11,28,29]. Our study revealed that ESD procedures performed by trainees are associated with the onset of PECS. A previous study showed that ESD procedures performed by trainees are longer than those performed by experienced endoscopists [23]. Because the swift-coagulation mode time probably increases as the procedure time lengthens, high Joule heat accumulation is likely to occur during long ESDs, causing severe damage to the peeled mucosal surface, leading to PECS. Previous studies were limited in that they did not consider the impact of the ESD procedure time on the Joule heat delivered to the lesion. In this study, measurement of swift-coagulation mode time allowed us to investigate the association between PECS and

Table 1 Characteristics of patients who underwent endoscopic submucosal dissection, *n* (%)

Patient features	*n* (%)
Number of patients	151
Male	94 (62.3)
Age (yr), mean ± SD	67.3 ± 10.9
BMI (kg/m^2), mean ± SD	22.9 ± 3.0
Specimen size	
< 40 mm	132 (87.4)
≥ 40 mm	19 (12.6)
Total Joule heat	
< 8460 J[1]	75 (49.7)
≥ 8460 J	76 (50.3)
Tumor location	
Right colon	59 (39.1)
Left colon	41 (27.1)
Rectum	51 (33.8)
Tumor morphology	
0-Is/Ip	29 (19.2)
LST-G	75 (49.7)
LST-NG (0-IIc)	47 (31.1)
Depth of pathological invasion	
Tis (M)	130 (86.1)
T1 (SM)	21 (13.9)
Histological diagnosis	
Adenoma	67 (44.4)
Adenocarcinoma	80 (53.0)
Other	4 (2.6)
ECOG performance status after ESD	
0	144 (95.4)
≥1	7 (4.6)
R0 resection	115 (76.2)
ESD procedure performed by trainees	52 (34.4)
Additional endoscopic therapy after ESD	2 (1.3)
Additional surgery after ESD	12 (7.9)
En bloc resection	135 (89.4)
Intraoperative perforation or penetration	7 (4.6)
Submucosal fibrosis	45 (29.8)
PECS	16 (10.6)

[1]Patients exposed to more or less than the median Joule heat value (8460 J) were assigned to the high and low Joule heat groups, respectively.
BMI: Body mass index; Is: Sessile type; Ip: Pedunculated type; LST-G: Lateral spreading tumor granular type; LST-NG: Lateral spreading tumor non-granular type; IIc: Superficial depressed type; Tis (M): Carcinoma in situ or intramucosal carcinoma; T1 (SM): Tumor invades submucosa; R0: Microscopically margin-negative; ESD: Endoscopic submucosal dissection; PECS: Post-endoscopic submucosal dissection electrocoagulation syndrome; SD: Standard deviation; ECOG performance status: Eastern Cooperative Oncology Group performance status.

total Joule heat. Our study revealed that the total Joule heat applied to the peeled

Table 2 Clinicopathological factors in the high and low Joule heat groups, *n* (%)

	High Joule heat	Low Joule heat	*P* value
	n = 76	*n* = 75	
Sex			0.54
Male	45 (59.2)	49 (65.3)	
Female	31 (40.8)	26 (34.7)	
Age (yr), mean ± SD	69 ± 11.5	66 ± 10.2	< 0.01
BMI (kg/m^2), mean ± SD	22.8 ± 2.3	23.0 ± 3.2	0.77
Specimen size			< 0.01
< 40 mm	60 (78.9)	73 (97.3)	
≥ 40 mm	16 (21.1)	2 (2.7)	
Tumor location			0.84
Right colon	28 (36.9)	31 (41.3)	
Left colon	21 (27.6)	20 (26.7)	
Rectum	27 (35.5)	24 (32.0)	
Tumor morphology			0.56
0-Is/Ip	18 (23.7)	21 (28.0)	
LST-G	36 (47.4)	29 (38.7)	
LST-NG (0-IIc)	22 (28.9)	25 (33.3)	
Depth of pathological invasion			0.66
Tis (M)	64 (84.2)	66 (88.0)	
T1 (SM)	12 (15.8)	9 (12.0)	
Histological diagnosis			0.12
Adenoma	34 (44.7)	33 (44.0)	
Adenocarcinoma	42 (55.3)	38 (50.7)	
Other	0 (0.0)	4 (5.3)	
Performance status after ESD			0.45
0	71 (93.4)	73 (97.3)	
≥ 1	5 (6.6)	2 (2.7)	
R0 resection	50 (65.8)	65 (86.7)	< 0.01
ESD procedure performed by trainees	37 (55.3)	15 (13.3)	< 0.01
Additional endoscopic therapy after ESD	1 (1.3)	1 (1.3)	0.999
Additional surgery after ESD	8 (10.5)	4 (5.3)	0.38
En bloc resection	69 (90.8)	73 (97.3)	0.18
Submucosal fibrosis	27 (35.5)	18 (24.0)	0.17
PECS	13 (17.1)	3 (4.0)	0.02

BMI: Body mass index; Is: Sessile type; Ip: Pedunculated type; LST-G: Lateral spreading tumor granular type; LST-NG: Lateral spreading tumor non-granular type; IIc: Superficial depressed type; Tis (M): Carcinoma in situ or intramucosal carcinoma; T1 (SM): Tumor invades submucosa; R0: Microscopically margin-negative; ESD: Endoscopic submucosal dissection; PECS: Post-endoscopic submucosal dissection electrocoagulation syndrome; SD: Standard deviation.

surface is involved in the development of PECS. Furthermore, using the total Joule heat cutoff value of PECS occurrence could allow the introduction of PECS prevention measures, including online measurement of swift-coagulation mode time during colorectal ESD. For example, an online PECS alert system is promising.

Table 3 Multivariate analysis of risk factors associated with high Joule heat accumulation

	Odds ratio	95%CI	*P* value
Age	1.03	0.99-1.06	0.17
R0 resection	3.27	1.26-8.45	0.01
Specimen size	1.07	1.03-1.11	< 0.01
ESD procedure performed by trainees	5.30	2.32-12.10	< 0.01
PECS	4.83	1.08-21.50	0.03

PECS: Post-endoscopic submucosal dissection electrocoagulation syndrome; R0: Microscopically margin-negative; 95% CI: 95% confidence interval.

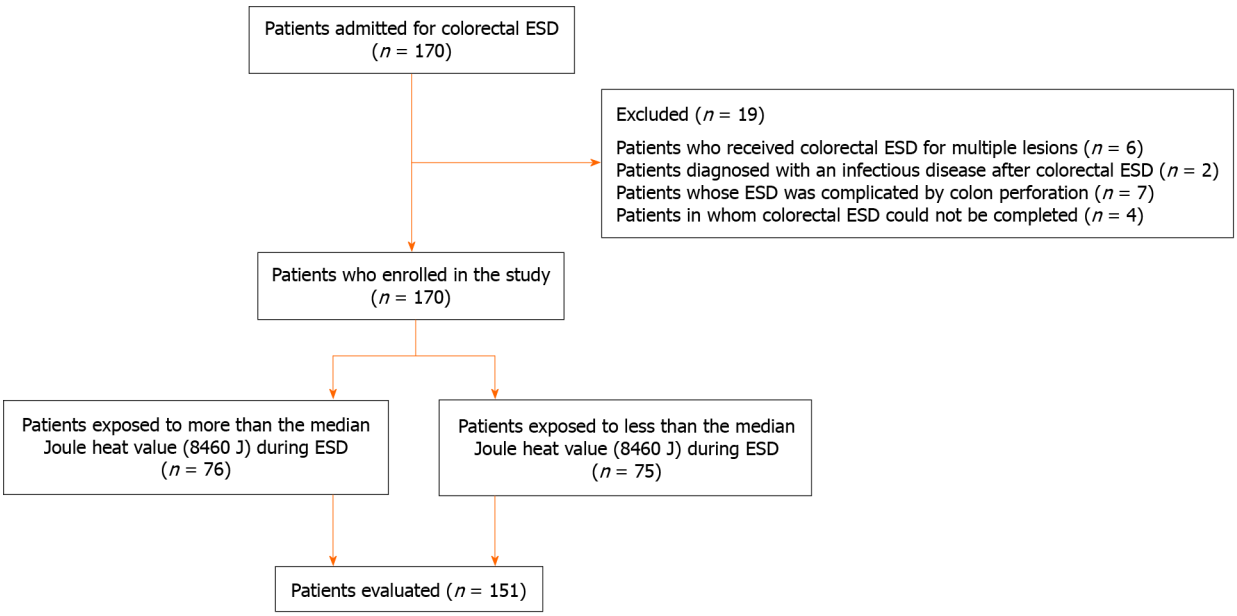

Figure 2 Study flowchart. ESD: Endoscopic submucosal dissection.

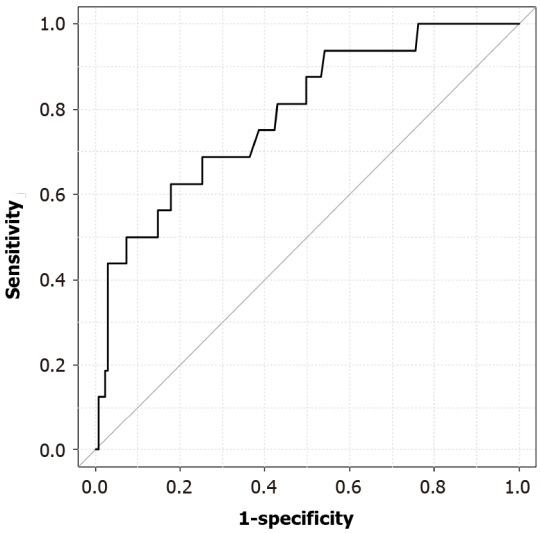

Figure 3 Receiver-operating characteristic curve showing the correlation between post-endoscopic submucosal dissection electrocoagulation syndrome and total Joule heat [area under the curve = 0.788 (95% confidence interval: 0.666-0.909)].

Limits of the study

First, because this was a retrospective cohort study, we could not rule out poor endoscope operability as a confounding factor. Second, as this was a single-center study, selection bias cannot be excluded. Nevertheless, we imposed strict inclusion and exclusion criteria to mitigate selection bias to the greatest extent possible. Last, the sample size was small. In the future, a prospective study should be performed to establish the validity of our results.

CONCLUSION

We found that Joule heat accumulation within the gastrointestinal wall is involved in the onset of PECS. ESD-related thermal damage to the mucosal peeled surface is probably a major component of the mechanism underlying PECS.

ARTICLE HIGHLIGHTS

Research background

Few studies have examined the impact of endoscopic submucosal dissection (ESD)-related thermal damage on the onset of post-ESD electrocoagulation syndrome (PECS).

Research motivation

We hypothesized that electrocoagulation is associated with Joule heat capable of causing thermal damage to the gastrointestinal wall during long ESD operations.

Research objectives

We aimed to determine the association between high Joule heat and the onset of PECS.

Research methods

We developed a novel device to measure the swift coagulation time with a sensor adjacent to the electrosurgical coagulation unit foot switch, which enabled us to calculate total Joule heat. PECS was defined as localized abdominal pain (visual analogue scale ≥ 30 mm during hospitalization or increased by ≥ 20 mm from the baseline) and fever (temperature ≥ 37.5 degrees or white blood cell count ≥ 10000 μ/L). Patients exposed to more or less than the median Joule heat value were assigned to the high and low Joule heat groups, respectively.

Research results

We evaluated 151 patients. The PECS incidence was 10.6% (16/151 cases), and all patients were followed conservatively and discharged without severe complications. In multivariate analysis, high Joule heat was an independent PECS risk factor. The area under the ROC curve showing the correlation between PECS and total Joule heat was high [0.788 (95% confidence interval: 0.666-0.909)].

Research conclusions

Joule heat accumulation in the gastrointestinal wall is involved in the onset of PECS. ESD-related thermal damage of the peeled mucosal surface is probably a major component of the mechanism underlying PECS.

Research perspectives

Future prospective studies should be performed to establish the validity of our results.

REFERENCES

1 **Puli SR**, Kakugawa Y, Saito Y, Antillon D, Gotoda T, Antillon MR. Successful complete cure *en-bloc* resection of large nonpedunculated colonic polyps by endoscopic submucosal dissection: a meta-analysis and systematic review. *Ann Surg Oncol* 2009; **16**: 2147-2151 [PMID: 19479308 DOI: 10.1245/s10434-009-0520-7]

2 **Saito Y**, Fukuzawa M, Matsuda T, Fukunaga S, Sakamoto T, Uraoka T, Nakajima T, Ikehara H, Fu KI, Itoi T, Fujii T. Clinical outcome of endoscopic submucosal dissection versus endoscopic mucosal

resection of large colorectal tumors as determined by curative resection. *Surg Endosc* 2010; **24**: 343-352 [PMID: 19517168 DOI: 10.1007/s00464-009-0562-8]

3 **Saito Y**, Uraoka T, Yamaguchi Y, Hotta K, Sakamoto N, Ikematsu H, Fukuzawa M, Kobayashi N, Nasu J, Michida T, Yoshida S, Ikehara H, Otake Y, Nakajima T, Matsuda T, Saito D. A prospective, multicenter study of 1111 colorectal endoscopic submucosal dissections (with video). *Gastrointest Endosc* 2010; **72**: 1217-1225 [PMID: 21030017 DOI: 10.1016/j.gie.2010.08.004]

4 **Kobayashi N**, Yoshitake N, Hirahara Y, Konishi J, Saito Y, Matsuda T, Ishikawa T, Sekiguchi R, Fujimori T. Matched case-control study comparing endoscopic submucosal dissection and endoscopic mucosal resection for colorectal tumors. *J Gastroenterol Hepatol* 2012; **27**: 728-733 [PMID: 22004124 DOI: 10.1111/j.1440-1746.2011.06942.x]

5 **Nakajima T**, Saito Y, Tanaka S, Iishi H, Kudo SE, Ikematsu H, Igarashi M, Saitoh Y, Inoue Y, Kobayashi K, Hisasbe T, Matsuda T, Ishikawa H, Sugihara K. Current status of endoscopic resection strategy for large, early colorectal neoplasia in Japan. *Surg Endosc* 2013; **27**: 3262-3270 [PMID: 23508817 DOI: 10.1007/s00464-013-2903-x]

6 **Wada Y**, Kudo SE, Tanaka S, Saito Y, Iishii H, Ikematsu H, Igarashi M, Saitoh Y, Inoue Y, Kobayashi K, Hisabe T, Tsuruta O, Kashida H, Ishikawa H, Sugihara K. Predictive factors for complications in endoscopic resection of large colorectal lesions: a multicenter prospective study. *Surg Endosc* 2015; **29**: 1216-1222 [PMID: 25159643 DOI: 10.1007/s00464-014-3799-9]

7 **Fujishiro M**, Yahagi N, Kakushima N, Kodashima S, Muraki Y, Ono S, Yamamichi N, Tateishi A, Oka M, Ogura K, Kawabe T, Ichinose M, Omata M. Outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms in 200 consecutive cases. *Clin Gastroenterol Hepatol* 2007; **5**: 678-683 [PMID: 17466600 DOI: 10.1016/j.cgh.2007.01.006]

8 **Isomoto H**, Nishiyama H, Yamaguchi N, Fukuda E, Ishii H, Ikeda K, Ohnita K, Nakao K, Kohno S, Shikuwa S. Clinicopathological factors associated with clinical outcomes of endoscopic submucosal dissection for colorectal epithelial neoplasms. *Endoscopy* 2009; **41**: 679-683 [PMID: 19670135 DOI: 10.1055/s-0029-1214979]

9 **Watabe H**, Yamaji Y, Okamoto M, Kondo S, Ohta M, Ikenoue T, Kato J, Togo G, Matsumura M, Yoshida H, Kawabe T, Omata M. Risk assessment for delayed hemorrhagic complication of colonic polypectomy: polyp-related factors and patient-related factors. *Gastrointest Endosc* 2006; **64**: 73-78 [PMID: 16813806 DOI: 10.1016/j.gie.2006.02.054]

10 **Okamoto K**, Watanabe T, Komeda Y, Kono T, Takashima K, Okamoto A, Kono M, Yamada M, Arizumi T, Kamata K, Minaga K, Yamao K, Nagai T, Asakuma Y, Takenaka M, Sakurai T, Matsui S, Nishida N, Chikugo T, Kashida H, Kudo M. Risk Factors for Postoperative Bleeding in Endoscopic Submucosal Dissection of Colorectal Tumors. *Oncology* 2017; **93** Suppl 1: 35-42 [PMID: 29258069 DOI: 10.1159/000481228]

11 **Jung D**, Youn YH, Jahng J, Kim JH, Park H. Risk of electrocoagulation syndrome after endoscopic submucosal dissection in the colon and rectum. *Endoscopy* 2013; **45**: 714-717 [PMID: 23990482 DOI: 10.1055/s-0033-1344555]

12 **Hong MJ**, Kim JH, Lee SY, Sung IK, Park HS, Shim CS. Prevalence and clinical features of coagulation syndrome after endoscopic submucosal dissection for colorectal neoplasms. *Dig Dis Sci* 2015; **60**: 211-216 [PMID: 25502119 DOI: 10.1007/s10620-014-3484-9]

13 **Yamashina T**, Takeuchi Y, Uedo N, Hamada K, Aoi K, Yamasaki Y, Matsuura N, Kanesaka T, Akasaka T, Yamamoto S, Hanaoka N, Higashino K, Ishihara R, Iishi H. Features of electrocoagulation syndrome after endoscopic submucosal dissection for colorectal neoplasm. *J Gastroenterol Hepatol* 2016; **31**: 615-620 [PMID: 26202127 DOI: 10.1111/jgh.13052]

14 **Lee SP**, Sung IK, Kim JH, Lee SY, Park HS, Shim CS, Ki HK. A randomized controlled trial of prophylactic antibiotics in the prevention of electrocoagulation syndrome after colorectal endoscopic submucosal dissection. *Gastrointest Endosc* 2017; **86**: 349-357.e2 [PMID: 27899322 DOI: 10.1016/j.gie.2016.11.022]

15 **Lee SP**, Kim JH, Sung IK, Lee SY, Park HS, Shim CS, Han HS. Effect of submucosal fibrosis on endoscopic submucosal dissection of colorectal tumors: pathologic review of 173 cases. *J Gastroenterol Hepatol* 2015; **30**: 872-878 [PMID: 25641510 DOI: 10.1111/jgh.12886]

16 **Hirasawa K**, Sato C, Makazu M, Kaneko H, Kobayashi R, Kokawa A, Maeda S. Coagulation syndrome: Delayed perforation after colorectal endoscopic treatments. *World J Gastrointest Endosc* 2015; **7**: 1055-1061 [PMID: 26380051 DOI: 10.4253/wjge.v7.i12.1055]

17 **Mori H**, Kobara H, Rafiq K, Nishiyama N, Fujihara S, Oryu M, Masaki T. Effects of gastric irrigation on bacterial counts before endoscopic submucosal dissection: a randomized case control prospective study. *PLoS One* 2013; **8**: e65377 [PMID: 23762354 DOI: 10.1371/journal.pone.0065377]

18 **Christie JP**, Marrazzo J 3rd. "Mini-perforation" of the colon--not all postpolypectomy perforations require laparotomy. *Dis Colon Rectum* 1991; **34**: 132-135 [PMID: 1993410 DOI: 10.1007/BF02049986]

19 **Nomura S**, Shimura T, Katano T, Iwai T, Mizuno Y, Yamada T, Ebi M, Hirata Y, Nishie H, Mizushima T, Nojiri Y, Togawa S, Shibata S, Kataoka H. A multicenter, single-blind randomized controlled trial of endoscopic clipping closure for preventing coagulation syndrome after colorectal endoscopic submucosal dissection. *Gastrointest Endosc* 2020; **91**: 859-867.e1 [PMID: 31785275 DOI: 10.1016/j.gie.2019.11.030]

20 **Arimoto J**, Higurashi T, Kato S, Fuyuki A, Ohkubo H, Nonaka T, Yamaguchi Y, Ashikari K, Chiba H, Goto S, Taguri M, Sakaguchi T, Atsukawa K, Nakajima A. Risk factors for post-colorectal

endoscopic submucosal dissection (ESD) coagulation syndrome: a multicenter, prospective, observational study. *Endosc Int Open* 2018; **6**: E342-E349 [PMID: 29527556 DOI: 10.1055/s-0044-101451]

21 **Lee H**, Cheoi KS, Chung H, Park JC, Shin SK, Lee SK, Lee YC. Clinical features and predictive factors of coagulation syndrome after endoscopic submucosal dissection for early gastric neoplasm. *Gastric Cancer* 2012; **15**: 83-90 [PMID: 21761134 DOI: 10.1007/s10120-011-0073-x]

22 **Tanaka S**, Kashida H, Saito Y, Yahagi N, Yamano H, Saito S, Hisabe T, Yao T, Watanabe M, Yoshida M, Saitoh Y, Tsuruta O, Sugihara KI, Igarashi M, Toyonaga T, Ajioka Y, Kusunoki M, Koike K, Fujimoto K, Tajiri H. Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection. *Dig Endosc* 2020; **32**: 219-239 [PMID: 31566804 DOI: 10.1111/den.13545]

23 **Hotta K**, Oyama T, Shinohara T, Miyata Y, Takahashi A, Kitamura Y, Tomori A. Learning curve for endoscopic submucosal dissection of large colorectal tumors. *Dig Endosc* 2010; **22**: 302-306 [PMID: 21175483 DOI: 10.1111/j.1443-1661.2010.01005.x]

24 **Freiberger H**. Der elektrische widerstand des menschlichen körpers gegen technischen gleich- und wechselstrom. Berlin: Verlag von Julius Springer, 1934

25 **Waye JD**, Lewis BS, Yessayan S. Colonoscopy: a prospective report of complications. *J Clin Gastroenterol* 1992; **15**: 347-351 [PMID: 1294644]

26 **Cha JM**, Lim KS, Lee SH, Joo YE, Hong SP, Kim TI, Kim HG, Park DI, Kim SE, Yang DH, Shin JE. Clinical outcomes and risk factors of post-polypectomy coagulation syndrome: a multicenter, retrospective, case-control study. *Endoscopy* 2013; **45**: 202-207 [PMID: 23381948 DOI: 10.1055/s-0032-1326104]

27 **Ito S**, Hotta K, Imai K, Yamaguchi Y, Kishida Y, Takizawa K, Kakushima N, Tanaka M, Kawata N, Yoshida M, Ishiwatari H, Matsubayashi H, Ono H. Risk factors of post-endoscopic submucosal dissection electrocoagulation syndrome for colorectal neoplasm. *J Gastroenterol Hepatol* 2018; **33**: 2001-2006 [PMID: 29864790 DOI: 10.1111/jgh.14302]

28 **Hanaoka N**, Uedo N, Ishihara R, Higashino K, Takeuchi Y, Inoue T, Chatani R, Hanafusa M, Tsujii Y, Kanzaki H, Kawada N, Iishi H, Tatsuta M, Tomita Y, Miyashiro I, Yano M. Clinical features and outcomes of delayed perforation after endoscopic submucosal dissection for early gastric cancer. *Endoscopy* 2010; **42**: 1112-1115 [PMID: 21120780 DOI: 10.1055/s-0030-1255932]

29 **Kobayashi R**, Hirasawa K, Sato C, Makazu M, Kaneko H, Ikeda R, Fukuchi T, Sawada A, Ozeki Y, Taguri M, Takebayashi S, Maeda S. Utility of multi-detector computed tomography scans after colorectal endoscopic submucosal dissection: a prospective study. *Gastrointest Endosc* 2018; **87**: 818-826 [PMID: 29122602 DOI: 10.1016/j.gie.2017.10.038]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com