Risk of Delayed Bleeding after Cold Snare Polypectomy in Patients with Antithrombotic Therapy

学　位　論　文

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Risk of Delayed Bleeding after Cold Snare Polypectomy in Patients with Antithrombotic Therapy

（抗血栓療法中の患者における大腸ポリープに対する非焼灼切除後の遅発性出血の危険性）

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ABSTRACT

Background

Cold snare polypectomy is being increasingly adopted, however there are few reports of cold snare polypectomy regarding antithrombotic therapy.

Aims

This study aimed to investigate the real-world safety of cold snare polypectomy during antithrombotic therapy.

Methods

We collected data from consecutive patients undergoing cold snare polypectomy in a single hospital between 2013 and 2017. Indications for cold snare polypectomy were any ≤10mm polyp. The primary outcome was delayed bleeding. We compared rates of delayed bleeding between patients with and without antithrombotic therapy and analyzed risk factors for delayed bleeding using binary logistic regression model with firth procedure.

Results

In 2152 patients (mean age 67.6 years; male 1411), 4433 colorectal polyps (mean diameter 5.0mm) underwent cold snare polypectomy. Clipping during the procedure was performed for 5.8%. Delayed bleeding occurred in 0.51% (11/2152) of patients and 0.25% (11/4433) of polyps, but no major delayed bleeding occurred. A total of 244 (11%) patients received antithrombotic therapy. Patients on antithrombotic therapy were older ($p<0.001$), more likely male ($p<0.001$) and had cold snare polypectomy in the proximal colon ($p=0.011$). The rate of delayed bleeding was higher in patients on antithrombotic therapy (1.64% vs. non-antithrombotic therapy 0.37%, $p=0.009$). Larger polyp size (>5mm), use of clips, and antithrombotic therapy were significant risk factors for delayed bleeding. There was no clear association between specific antithrombotic agents and delayed bleeding.

Conclusions

Delayed bleeding after cold snare polypectomy was rare even in patients with antithrombotic therapy, and no major delayed bleeding occurred.

Key Words: colonoscopy; colonic polyp; cold snare polypectomy; antithrombotic agent; delayed hemorrhage

Abbreviations：

CSP: cold snare polypectomy

ATT: antithrombotic therapy

ESGE: European Society of Gastrointestinal Endoscopy

ASGE: American Society for Gastrointestinal Endoscopy

JGES: Japan Gastroenterological Endoscopy Society

INR: international normalized ratio

DOAC: direct oral antithrombotic agent

RCT: randomized control trial

STROBE: Strengthening the reporting of observational studies in epidemiology

Introduction

Cold snare polypectomy (CSP) for diminutive polyps was initially reported in 1992[1] and is being increasingly adopted due to its ease and low rate of complications, particularly delayed bleeding. Any bleeding at the resection site after CSP almost invariably stops spontaneously. The incidence of delayed bleeding in a large trial was zero in 1015 sub-centimeter polyps [2]. The low rate of delayed bleeding is likely related to superficial submucosal damage with CSP [3] and subsequent early mucosal healing after CSP [4].

Recently, the American Society for Gastrointestinal Endoscopy (ASGE) and the European Society of Gastrointestinal Endoscopy (ESGE) have recommended CSP as the preferred technique for removing diminutive polyps ≤5mm. Both of the associations also suggest CSP for sessile polyps of 6–9mm in size because of its superior safety profile, although acknowledged that evidence comparing efficacy with conventional hot snare polypectomy is lacking [5]. In contrast, the Japan Gastroenterological Endoscopy Society (JGES) have not made similar recommendations.

The number of colonoscopy patients taking anticoagulants and/or antiplatelet agents for the treatment or prevention of cardiovascular or cerebrovascular disease is increasing [6,7]. Current guidelines regard hot snare polypectomy as a high-risk procedure for bleeding, even if antithrombotic therapy (ATT) has been temporally discontinued [8]. Two reports have shown that patients taking antithrombotic agents are more prone to postpolypectomy bleeding than those not taking antithrombotic agents [9,10].

There are subtle differences among guidelines internationally as shown in Table 1. The 2012 JGES guidelines [11] recommend hot snare polypectomy with a short interruption of antithrombotic medication, and warfarin can be continued if the international normalized ratio (INR) is within the therapeutic range (less than 3.0). The ASGE guidelines recommend that aspirin is continued, and that warfarin is held for 5 days [12]. ESGE also advocates similar recommendation to hold warfarin for 5 days and to stop direct oral antithrombotic agent (DOAC) for 48 hours. In general, guidelines recommend stopping thienopyridines 5 days before the procedure.

Can we safely apply CSP for patients receiving ATT? None of the guidelines refer to periprocedural antithrombotic management for CSP. In 2014, Horiuchi et al reported in a randomized control trial (RCT) that CSP causes no delayed bleeding even in patients receiving warfarin [13]. In 2019, Takeuchi et al reported in an RCT that patients with CSP for subcentimeter colorectal polyps who were receiving warfarin or DOACs did not have an increased incidence of polypectomy-related major bleeding [14]. As for antiplatelet therapy, Chan et al reported in an RCT that a slightly larger proportion of patients continuing thienopyridine developed delayed postpolypectomy bleeding, but this difference was not statistically significant [15]. Also, latest retrospective study on only 109 patients with ATT showed that continued use of antithrombotic agents did not increase the risk of delayed bleeding [16]. To date, there are a few real-world data on CSP for the patients with ATT. Hence, we conducted an observational cohort study to investigate the safety of CSP for patients receiving ATT.

Methods

Study Design

We conducted a single-center, observational study. The study was reviewed and approved by the Institutional Review Board at Fukushima Medical University (registration No.29147). All data were collected by October 2019. The STROBE (Strengthening the reporting of observational studies in epidemiology) guidelines were followed in reporting this study.

Subjects

Consecutive patients who underwent CSP from May 2013 and December 2017 at the Aizu Medical Center were enrolled. Prior to study commencement, the Institutional Review Board

approved the study and waived the requirement for informed consent. Information including short-term outcomes was obtained from medical records.

Colonoscopic Procedure

Patients who are scheduled to undergo colonoscopy were normally prepared on the premise of receiving polypectomy in our institution. The decision to continue or discontinue ATT medication followed the JGES guidelines, which are similar to those of the ASGE and ESGE (Table 1) with the exception of aspirin (discontinued) and warfarin (continued, if INR<3). In patients receiving multidrug therapy, decision of each antithrombotic agents was primarily made through consultation with the prescribing doctor. Based on adherence to the JGES guideline, the ATT group was stratified into three subgroups: (a) patients who strictly adhered to the guidelines by temporarily ceasing or holding their ATT ("Adhere to the guideline" group), (b) patients who held their ATT longer than recommended by the guideline ("Long discontinuation" group), and (c) patients who continued their ATT shorter than recommended by the guideline ("Short discontinuation" group). Patients who did continue their ATT or who were on heparin-bridge were included in the "Short discontinuation" group. Nursing staff instructed the duration of holding their ATT at the time of scheduling colonoscopy, and they confirmed if the patients strictly followed the instruction on the day of colonoscopy. Patients received polyethylene glycol bowel preparation beginning the day before the procedure. Typically, patients were given an anticholinergic agent or glucagon by intramuscular injection and received intravenous sedation if necessary. Colonoscopy was performed by using the scopes with optical magnification apparatus (model PCF-H290AZI, HQ290I; Olympus Medical System, Tokyo, Japan, model EC-L600ZP, EC-L590ZW; Fujifilm, Tokyo, Japan), and magnified observation was made at the endoscopists' discretion.

Polyps measuring 2-10mm were resected by CSP, regardless of morphology and including pedunculated polyps, except for lesions with colonoscopic findings suspicious for invasive cancer

or high-grade dysplasia which were not removed using CSP. Serrated lesions ≥5 mm in the proximal colon were resected with CSP. In order to assess polyp size, an open-biopsy forceps was primarily used as standard. The snare used for CSP were Captivator™13mm (Boston Scientific, Marlborough, US) and Snare Master 10mm (Olympus, Tokyo, Japan). The technique used was cold resection of the polyp without tenting and then suction of the transected polyp into a trap followed by submission for histopathologic evaluation. Hemostatic clips were applied for active bleeding, such as spurting or oozing that lasted for more than one minute after polypectomy. Prophylactic clipping of resection sites was permitted at the endoscopists' discretion. Patients started their ATT medication the next day, if their bleeding was not observed. All patients were reviewed within one month of polypectomy in the outpatient clinic, to inform them of the histology and to evaluate for the occurrence of delayed bleeding. Patients were also questioned about other gastrointestinal symptoms, adherence to the instruction of their ATT, and any adverse events including perforation.

Outcome Measures

The primary outcome measure was the rate of delayed bleeding, defined as "hematochezia occurring within 2 weeks of CSP and with the resection site confirmed endoscopically as the bleeding source". We had a liberal repeat colonoscopy strategy, including all patients admitted with bleeding, and outpatients with frequent or suspected hematochezia. We compared rates of delayed bleeding between ATT group and non-ATT group, and also between ATT continuation group and ATT discontinuation group. Secondary outcome measures were the rate of clip application and patient and polyp-based risk factors for delayed bleeding.

Statistical Methods

This observational study was exploratory, and we did not calculate or pre-specify a sample size. For nominal data, statistical comparisons used a chi-square test. For continuous data, one-way ANOVA was applied if appropriate. To investigate risk factors for delayed bleeding, binary logistic regression analyses using firth procedures were applied because events (delayed bleeding) were rare. Firth procedure provides bias-reduction for small sample size as well as yields finite and consistent estimates even in case of separation. Covariates of per-patients analysis are age, gender, ATT and number of polyps resected. Covariates of per polyp analysis are size, location, morphology, histology, and presence of clipping. All p values are two-tailed, and values <0.05 were considered to indicate statistical significance. All statistical analyses were performed with Stata 16.1™ (Stata Corp., TX, United States).

Results

Patient flow (Figure 1)

A total of 7693 colonoscopies were performed, and 3036 patients underwent polypectomy. After excluding 884 patients who received hot resection alone, 4433 colorectal polyps (mean diameter 5.0±1.9mm) in 2152 patients (mean age 67.6±10.9; male 1: female 0.52) were resected with CSP and enrolled. Among these patients, 244 (11%) had received ATT (ATT group) whereas the remaining 1908 (89%) had not received ATT (non-ATT group). Based on adherence to the JGES guideline, the ATT group was stratified into “adhered to the guideline” group (65%), “long discontinuation” group (18%), and “short discontinuation” group (17%). To evaluate continuation of ATT, we separately stratified the ATT group into a “ATT discontinuation” group (69%) and a “ATT continuation” group (31%). And subsequently, the “Adherence to the guideline” group was divided into an ATT discontinuation or continuation group.

Background Characteristics of Patients and Polyps (Table 2)

A total of 244 patients (11%) were in the ATT group and 1908 patients (89%) were in the non-ATT group. The ATT group comprised statistically more males and were older. The number of polyps resected per person was equivalent between two groups. Antithrombotic agents included antiplatelet agents in 65.2%, anticoagulants in 30.7% and combined (antiplatelet and anticoagulant) drugs in 4.1%. In the ATT group, 13 patients (8 on anticoagulants and 5 on antiplatelets) received heparin-bridge therapy during the periprocedural period, because previous colonoscopy confirmed polyps to be resected.

A total of 512 (12%) polyps resected by CSP were in ATT group, and the remaining 3921 (88%) polyps were in non-ATT group. There were more proximal lesions (p=0.011), more low-grade adenoma (p=0.023) in the ATT group, compared with the non-ATT group. The rate of clip application in the ATT group was significantly higher than the non-ATT group (<0.001%). In contrast, there were no significant differences in polyp size or morphology between the two groups.

Delayed Hemorrhage Rates

The rates of delayed bleeding in the ATT group were 1.64% (4 of 244) of patients (patient-based analysis, Fig. 2A) and 0.78% (4 of 512) of polyps (polyp-based analysis, Fig. 2B). The rates were significantly higher than in the non-ATT group (per patient p=0.009, per polyp p=0.010). All delayed bleeding in the ATT group occurred in patients who had strictly adhered to the JGES guidelines. No delayed bleeding occurred in the 13 patients who received heparin-bridge therapy. In comparison between continuation and discontinuation of ATT during periprocedural period, there were no significant differences per-patient (Fig. 2C) and per-polyp analyses (Fig. 2D).

Risk factors for Delayed Hemorrhage

The analyses of risk factors for delayed bleeding are shown in Table 3. Univariate/multivariate logistic regression analysis using firth procedure showed that ATT was only

a risk factor in the per patient analysis. Old age (≥65 year) was a possible protective factor in the univariate (p=0.124) and also multivariate (p=0.050) analysis. In the per polyp analysis, univariate analysis showed that polyp size (>5mm), morphology (0-Ip) and use of clips were significant risk factors, but multivariate analysis showed that polyp size (>5mm) and use of clips were significant risk factors. Delayed bleeding rate was higher in multidrug therapy compared with monotherapy, but the difference was not statistically significant (p=0.404). There was no clear association between delayed bleeding and a specific antithrombotic agent (Table 4).

Bleeding Cases (Table 5)

Overall, 11 patients experienced delayed bleeding, which occurred on the day after CSP in 9, and within 3 days in the remaining 2. Delayed bleeding did not result in serious adverse events, with no blood transfusion or surgical intervention required. All patients in the ATT group (n=4) with delayed bleeding were male and aged 72 years or less, and after resection of low-grade adenomas that were 8-10 mm in size. One example of delayed bleeding in the ATT group is shown in Figures 3A, 3B and 3C. 70-year-old male who had withheld aspirin for 3 days underwent CSP for an 8mm sessile (0-IIa) adenoma in the transverse colon (A). Immediate bleeding occurred just after resection (B), and this was treated with one clip. Two days later, delayed bleeding occurred. Colonoscopy confirmed the previous resection site to be the bleeding source (C). Delayed bleeding was successfully treated by hemostatic clipping again. No blood transfusion was required.

Discussion

In this retrospective cohort study, we have shown that delayed bleeding after CSP is rare even in patients receiving ATT, and that major bleeding does not occur. However, ATT was a risk factor for delayed bleeding, irrespective of temporary discontinuation.

Our study represents, to our knowledge, the largest series of CSP patients among both real-world (non-clinical trial) studies and clinical trials. Compared to previous reports in which delayed bleeding did not occur, we do report an incidence, albeit rare, of delayed bleeding after CSP. In Repici's study [2], delayed bleeding was not observed in any of 823 patients with 1053 CSPs. And more recently, real-world studies from Japan [17-19] also demonstrated no delayed bleeding, while in Taiwan, only one minor delayed bleeding occurred among 1255 patients (bleeding rate 0.08%) [20]. The latest systematic review of clinical trials showed a delayed bleeding rate of 0.98% (10 of 1021 polyps) after CSP, but neither blood transfusion nor surgical intervention were required in any patient [21]. These observations indicate that delayed bleeding occurs infrequently after CSP and is minor.

In our study, independent risk factors for delayed bleeding were larger polyp size (>5mm), use of clips and ATT. These risk factors are similar those reported for conventional hot snare resection. In contrast, we did not observe an effect of polyp location; proximal colon is a known independent risk factor for delayed bleeding after hot resection [22, 23].

Polyp size is a well-known risk factor for conventional hot snare polypectomy [22, 24]. We found delayed bleeding after cold snare resection occurred only in lesions >5mm in size. Notably, all delayed bleeding happened in polyps measuring 8-10 mm in the ATT group.

With conventional hot polypectomy, an increased risk of delayed bleeding has been seen with thienopyridines [25, 26], and after the use of heparin-bridge therapy [27, 28]. However, in our study of CSP, we observed a higher rate of delayed bleeding with ATT, but it did not occur more often with any particular antithrombotic agent including multidrug therapy, and we did not observe delayed bleeding in any of the 13 patients receiving heparin-bridge therapy. However, we have to pay attention to these observations because this study did not handle so large number of ATT patients.

Old age could be a risk factor for post-polypectomy delayed bleeding due to atherosclerosis of the blood vessels [29]. In our study however, younger age (<65 years) was a possible risk factor for delayed bleeding after CSP (p=0.050, multivariate analysis). In a recent meta-analysis [19],

cardiovascular disease, hypertension, polyp size > 10 mm, and proximal colon location were significant risk factors for delayed bleeding, but age was not. In a further large-scale (3887 patients) prospective study of hot resection from Korea, young age (<50 years), aspirin use, polyp size, and immediate bleeding were independent risk factors for delayed post-polypectomy bleeding [30]. It might be attributed that most young patients immediately return to their normal life, e.g., drinking alcohol and exercise such as jogging.

In general, immediate bleeding after CSP invariably stops spontaneously and does not require hemostatic clipping [1]. While prophylactic clipping has not been consistently effective for preventing delayed bleeding after hot snare polypectomy, independent of receiving ATT [31-33], hemostatic clips are effective for control of immediate bleeding after polypectomy [34]. In our series, clipping for either hemostatic or prophylactic indications were permitted at the colonoscopists' discretion, and we observed that clips were applied more frequently in patients on ATT. This is likely because colonoscopists chose to apply clips prophylactically more often in this context, and also, because of any post-CSP, immediate bleeding may have prompted the use of clips for hemostasis. The use of clips may therefore have been a surrogate marker for immediate bleeding, which is a known risk factor for delayed bleeding [19].

This study has several acknowledged limitations. First, this is a retrospective study, and subject to selection bias. Due to retrospective analysis, we were not able to know the rate of immediate bleeding, which is a possible risk factor for delayed bleeding. Second, six colonoscopists with a wide range of experience performed the procedures; with a wide variation in application in prophylactic/hemostatic clipping and management of patients during periprocedural period may show a wide variation. Third, only 244 patients on ATT may not be sufficient to analyze the risk factors for delayed bleeding after CSP. Therefore, we had to use firth procedures due to the rare events of delayed bleeding. Fourth, the generalizability of our findings may be limited, Asians are known to have a different tendency of coagulability [35, 36]. Our study represents, to our knowledge, the largest series of CSP patients among both real-world studies and clinical trials.

In conclusion, CSP can be safely performed even in patients receiving ATT. Minor delayed bleeding does occur after CSP, especially in patients on ATT. Large polyp size, use of clips for immediate bleeding, and ATT were risk factors for delayed bleeding after CSP.

Author's contribution:

Acquisition of data: Aizawa, Nemoto, Utano, Isohata, Endo, Togashi

Interpretation of data: Aizawa, Nemoto, Utano, Tanaka, Togashi

Drafting of the manuscript: Aizawa, Togashi

Critical revision of the manuscript for important intellectual content: Aizawa, Nemoto, Utano, Isohata, Endo, Tanaka, Hewett, Togashi

Statistical analysis: Aizawa, Nemoto, Togashi, Tanaka

Obtained funding: Togashi

Administrative, technical, or material support: Hewett, Togashi

Study supervision: Hewett, Togashi

Final manuscript approval: Aizawa, Nemoto, Utano, Isohata, Endo, Tanaka, Hewett, Togashi

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Table 1. Management of patients receiving antithrombotic therapy

	JGES (2014)	ASGE (2016)	ESGE (2017)
Aspirin	Hold for 3-5 days Hold for 5-7 days	Continue	Continue
Thienopyridine	Or replace into Aspirin/Cilostazol	Hold for 5-7 days	Hold for 5-7 days
Cilostazol	Hold for 2 days	Hold for 2 days	Hold for 2 days
Warfarin	"INR <3.0 " is permitted	Hold for 5 days	Hold for 5 days
DOAC	Discontinue at the day	Discontinue at the day	Hold for 2 days

JGES: Japan Gastroenterological Endoscopy Society

ASGE: American Society for Gastrointestinal Endoscopy

ESGE: European Society of Gastrointestinal Endoscopy

DOAC: direct oral anticoagulant

Table 2. Features of Patients and Polyps

		ATT group	Non-ATT group	p value
Patient		N=244	N=1908	
gender n (%)	female	57 (23.4%)	684 (35.8%)	<0.001*
	male	187 (76.6%)	1224 (64.2%)	
age, year	mean SD	72.7±7.8	66.9±11.1	<0.001**
antithrombotic agents, n (%)	antiplatelet	159 (65.2%)	0 (0%)	N/A
	anticoagulant	75 (30.7%)	0 (0%)	N/A
	combined	10 (4.1%)	0 (0%)	N/A
No. of polyps resected		2.10±1.49	2.05±1.42	0.294**
Polyp		N=512	N=3921	p value
diameter (mm)	mean ± SD	4.99 ± 1.93	5.00 ± 1.87	0.296**
morphology †, n (%)	0-IIa	187 (36.5%)	1459 (37.2%)	0.519*
	0-Is	318 (62.1%)	2381 (60.7%)	
	0-Ip	7(1.4%)	81 (2.1%)	
location, n (%)	proximal colon	323 (63.1%)	2199 (56.1%)	0.011*
	distal colon	155 (30.3%)	1405 (35.8%)	
	rectum	34 (6.6%)	317 (8.1%)	
histology, n (%)	HGA	2 (0.4%)	31 (0.8%)	0.023*
	LGA	435 (85.0%)	3169 (80.8%)	
	Serrated lesions	26 (5.1%)	346 (8.8%)	
	Others ‡	49 (9.6%)	375 (9.6%)	
clipping rate, n (%)		52 (10.2%)	204 (5.2%)	<0.001*

ATT, antithrombotic therapy; SD, standard deviation; HGA, high grade adenoma; LDA, low grade adenoma; N/A, not applicable

† Morphology is classified by Paris' classification.

‡ Others include inflamed mucosa, inflammatory polyp, miscellaneous polyps and unable to retrieve.

* chi-square test ** one-way ANOVA

Table 3. Risk factors for delayed hemorrhage

		Univariate		Multivariate	
		OR (95%CI)	p-value	OR (95%CI)	p-value
Patient factor					
age, year	≥65	0.40 (0.12-1.29)	0.124	0.29 (0.085-1.00)	0.050
gender	male	2.00 (0.50-8.09)	0.329	1.47 (0.35-6.11)	0.595
ATT	present	4.74 (1.46-15.38)	0.009	6.11 (1.76-21.25)	0.004
No. of polyps resected	>2	1.24 (0.92-1.69)	0.160	1.21 (0.89-1.64)	0.216
Polyp factor					
size	>5mm	47.18 (2.78-801.25)	0.008	37.38 (2.16-644.73)	0.013
location	proximal colon	0.90 (0.29-2.79)	0.849	0.94 (0.30-2.96)	0.092
morphology †	0-Ip	7.08 (1.26-39.68)	0.026	2.82 (0.49-16.22)	0.245
histology	HGA	3.13 (0.18-53.81)	0.431	1.75 (0.09-32.89)	0.707
clipping	present	9.91 (3.06-31.11)	<0.001	4.95 (1.52-16.10)	0.008

OR, odds ratio; CI, confidence interval; ATT, antithrombotic therapy; HGA, high grade adenoma

† Morphology is classified by Paris' classification.

Table 4. Antithrombotic Therapy and Delayed Hemorrhage Rates

	n (%)	Delayed Hemorrhage (%)
Monotherapy	216 (88.5%)	3 (1.4%)
antiplatelet agent	141 (57.8%)	2 (1.4%)
Aspirin	68 (27.9%)	1 (1.5%)
THI	10 (4.1%)	0 (0.0%)
Cilostazol	22 (9.0%)	0 (0.0%)
others §	41 (16.8%)	1 (2.4%) †
anticoagulant agent	75 (30.7%)	1 (1.3%)
Warfarin	29 (11.9%)	1 (3.4%)
DOAC	46 (21.3%)	0 (0.0%)
Multidrug Therapy	28 (11.4%)	1 (3.6%) ‡
aspirin+THI	15 (6.1%)	1 (6.7%)
aspirin + warfarin	4 (1.6%)	0 (0.0%)
aspirin + DOAC	2 (0.8%)	0 (0.0%)
aspirin + cilostazol	1 (0.4%)	0 (0.0%)
cilostazol + warfarin	2 (0.8%)	0 (0.0%)
THI + others	1 (0.4%)	0 (0.0%)
warfarin + others	1 (0.4%)	0 (0.0%)
aspirin + THI + warfarin	1 (0.4%)	0 (0.0%)

DOAC, direct oral anticoagulant; THI, thienopyridine

† Patient taking dipyridamole

‡ Patient taking aspirin and thienopyridine

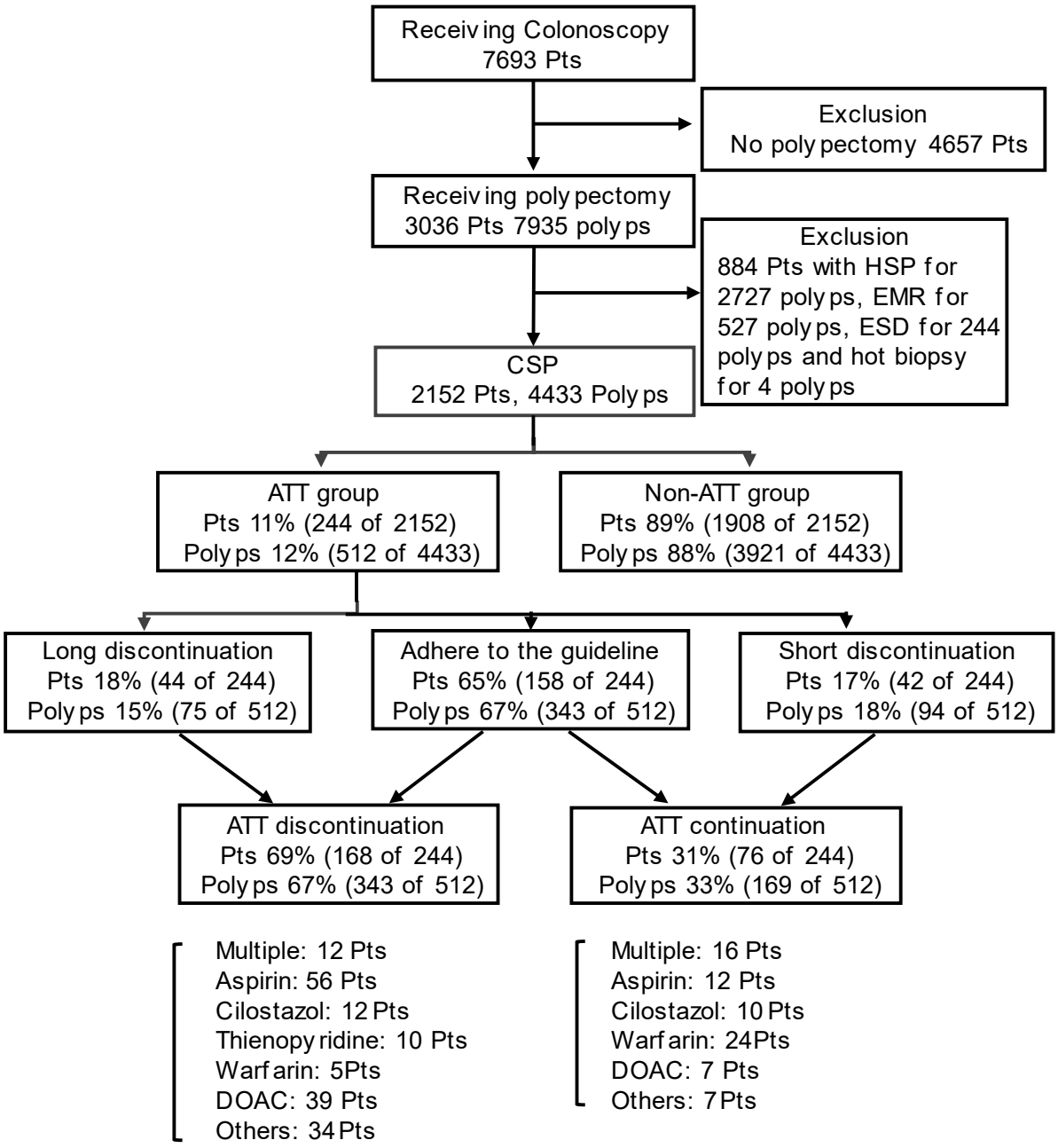
§ Others were dipylidamole, ethyl icosapentate, limaprost alfadex, trapidil etc.

Table 5. Delayed Bleeding Cases

ATT	Age	Gender	Location	Morphology	Size (mm)	Clipping	Histology	Days to hemorrhage
aspirin+thienopiridine	61	male	left	0-Is	9	done	LGA	2
aspirin	70	male	right	0-Is	8	done	LGA	1
dipyridamole	69	male	left	0-Is	10	done	LGA	1
warfarin	72	male	right	0-IIa	10	no	LGA	1
none	47	male	right	0-Is	9	done	LGA	3
none	52	female	right	0-Ip	6	no	LGA	1
none	78	male	left	0-Is	6	no	LGA	1
none	47	male	left	0-Is	10	no	LGA	1
none	63	male	right	0-Is	8	no	LGA	1
none	55	male	left	0-IIa	6	no	LGA	1
none	63	female	left	0-Is	8	no	LGA	1

ATT, antithrombotic therapy; LGA, low-grade adenoma.

Figure.1 Study flow diagram



Pts: patients; CSP: cold snare polypectomy; HSP: hot snare polypectomy;

EMR: endoscopic mucosal resection; ESD: endoscopic submucosal dissection;

ATT: antithrombotic therapy

Fig. 2A. Delayed hemorrhage rates by ATT (based on patient)

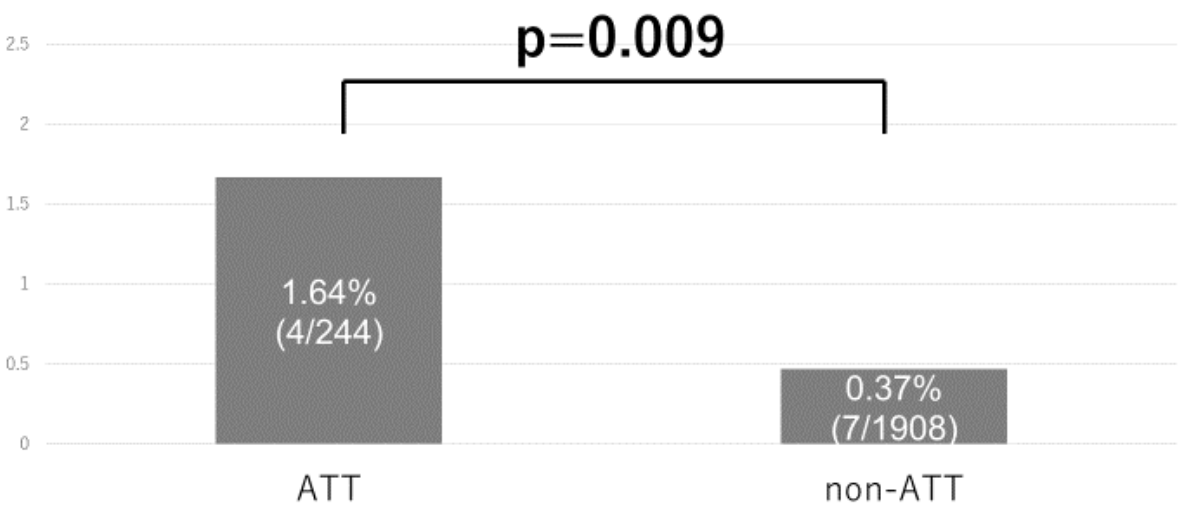


Fig. 2B. Delayed hemorrhage rates by ATT (based on polyp)

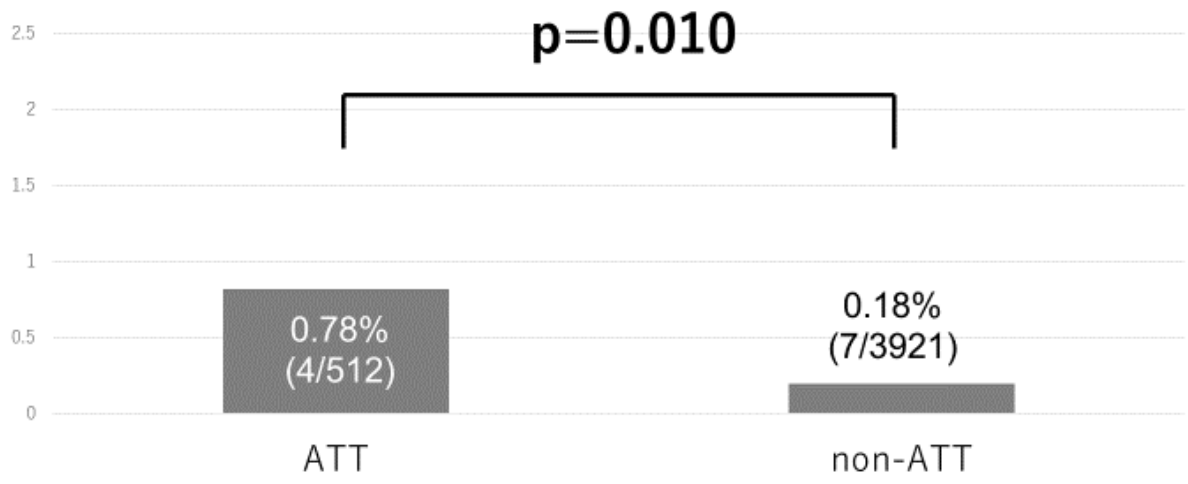


Fig. 2C. Delayed hemorrhage rates by continuation of ATT (based on patient)

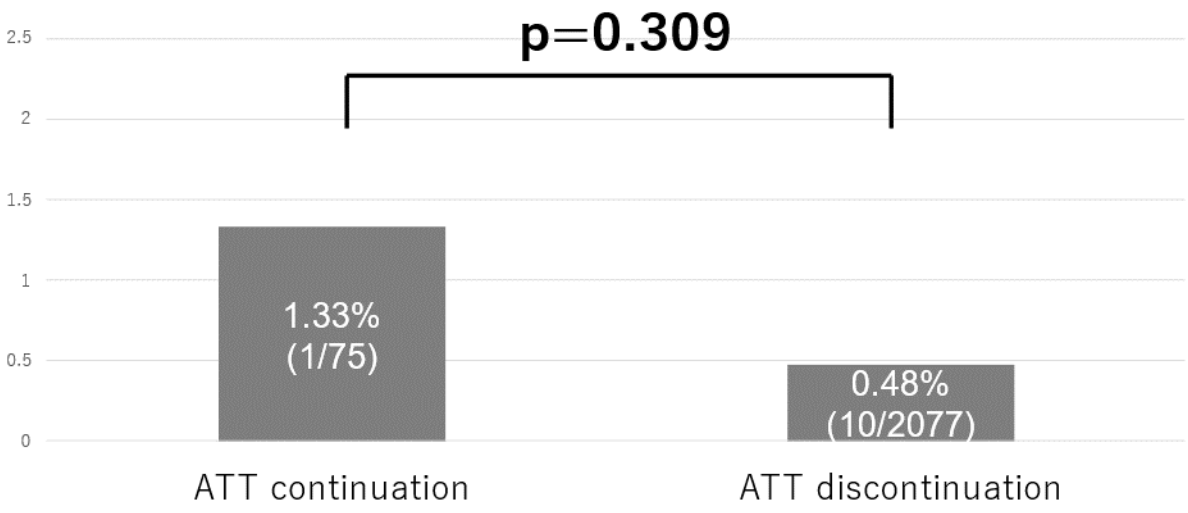


Fig. 2D. Delayed hemorrhage rates by continuation of ATT (based on polyp)

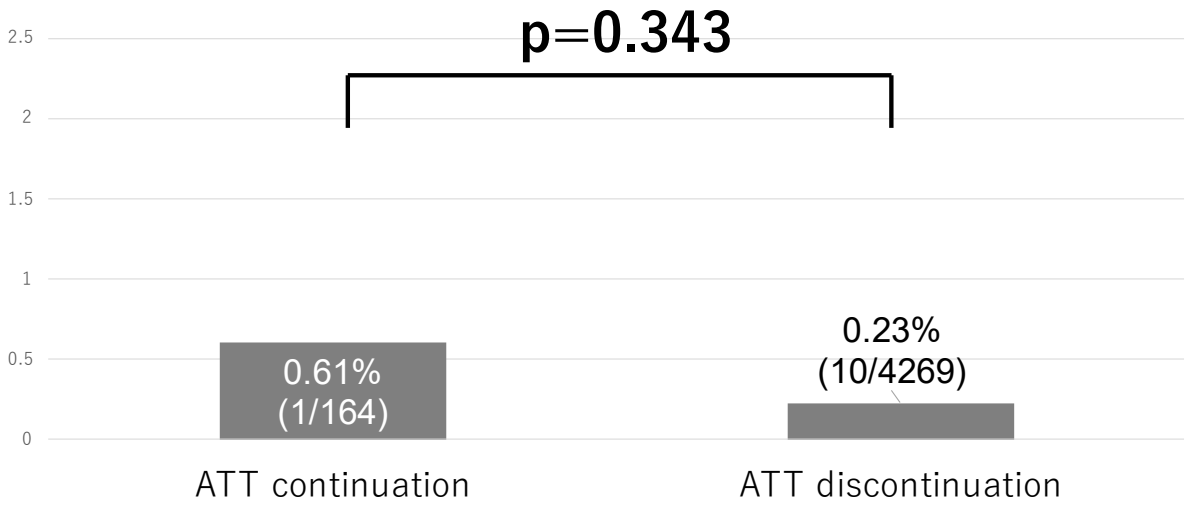


Figure 3A. Delayed Bleeding Case. A 70 y.o. man withheld aspirin, T-colon 8mm IIa

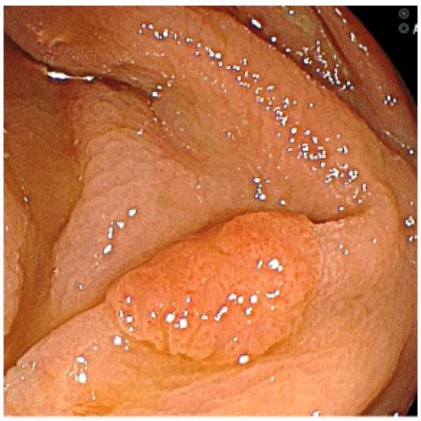


Figure 3B. Immediate bleeding was stopped with hemostatic clipping.

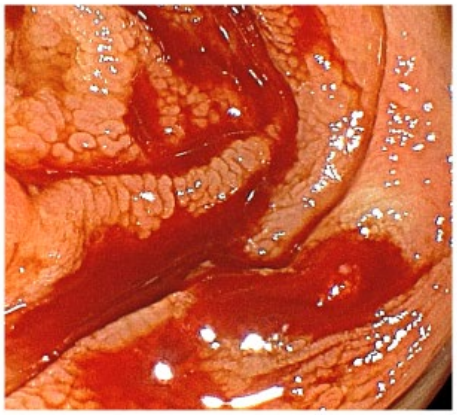


Figure 3C. Two days later, delayed bleeding occurred and successfully treated by hemo-clipping again.