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Original Article

Effect of Antithrombotic Therapy on Bleeding after Argon Plasma Coagulation for Gastric Neoplasms

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Background/Aims: Postprocedural bleeding is known to be relatively low after argon plasma coagulation (APC) for gastric neoplasms; however, there are few studies proving the effect of antithrombotic agents. This study aimed to analyze the incidence of delayed bleeding (DB) based on antithrombotic agents administered and to identify the risk factors for DB in APC for gastric tumors.

Methods: A total of 785 patients with 824 lesions underwent APC for single gastric neoplasm between January 2011 and January 2018. After exclusion, 719 and 102 lesions were classified as belonging to the non-antithrombotics (non-AT) and AT groups, respectively. The clinical outcomes were compared between the two groups, and we determined the risk factors for DB in gastric APC.

Results: Of the total 821 cases, DB occurred in 20 cases (2.4%): 17 cases in the non-AT group and three cases in the AT group (2.4% vs 2.9%, p=0.728). Multivariate analysis of the risk factors for DB confirmed the following significant, independent risk factors: male sex (odds ratio, 7.66; 95% confidence interval, 1.02 to 57.69; p=0.048) and chronic kidney disease (odds ratio, 4.51; 95% confidence interval, 1.57 to 13.02; p=0.005). Thromboembolic events and perforation were not observed in all patients regardless of whether they took AT agents.

Conclusions: AT therapy is acceptably safe in gastric APC because it does not significantly increase the incidence of DB. However, patients with chronic kidney disease or male sex need to receive careful follow-up on the incidence of post-APC bleeding. **(Gut Liver 2022;16:198-206)**

Key Words: Antithrombotic therapy; Argon plasma coagulation; Stomach neoplasm

INTRODUCTION

Argon plasma coagulation (APC) is a contact-free electrocoagulation method which transfers high-frequency electric current through ionized argon gas to targeted lesions.[1-3] According to the development of therapeutic endoscopy, APC also has been used to treat patients with several gastric neoplastic lesions.[4-7] Previous studies have reported that APC is safer than endoscopic submucosal dissection (ESD) regarding complications such as bleeding.[5,8-10] However, unlike ESD, few studies have evaluated risk factors of postprocedural bleeding after APC because of their low complication rate.

With the increase in the use of antithrombotic agents, the management of these drugs during the perioperative period has remained a great concern. Patients with antithrombotic therapy have potential risk for bleeding. However, contrary to gastric ESD, American and Asian Pacific guidelines[11,12] do not recommend withholding antithrombotic agents in low-risk procedures, including APC.

Until now, few studies with a small number of patients have reported the effects of antithrombotic agents on post-APC bleeding. In addition, because of the evolution and variety of antithrombotic agents, the management of antithrombotic therapy during the perioperative period of gastric APC has remained unclear.

The aim of this study was to compare the delayed bleeding (DB) rate during the perioperative period of gastric

APC among patients receiving antithrombotic therapy with those not receiving antithrombotic therapy. In addition, we also identified the risk factors of DB in gastric APC.

MATERIALS AND METHODS

1. Patients and lesions

Patients with a single gastric tumor who underwent APC from January 2011 to January 2018 were retrospectively reviewed at Asan Medical Center, Seoul, Korea. During this period, a total of 785 patients with 824 lesions had undergone APC. Of them, two hyperplastic polyps and one neuroendocrine tumor were excluded. After exclusion, 719 lesions were not exposed to antithrombotic therapy, whereas 102 lesions were exposed (Fig. 1). We compared the clinical outcomes between the two groups. Informed consent was obtained from all patients before the procedure. The Institutional Review Board of Asan Medical Center approved this study (IRB number: 2014-0894).

2. Endoscopic procedure

APC treatment was performed when the gastric neoplasms of less than 1 cm confined to mucosa, or when the patients or lesions met the following criteria: (1) when the patient is elderly or unable to perform long-term procedure due to poor cooperation; (2) when the patient has high risk conditions such as severe coagulopathy or heart failure; or (3) when the lesions are untreatable by endoscopic resection because of unclear margins, non-lifting sign, or technically difficult area. Patients were under conscious sedation with intravenous midazolam (0.05 mg/kg) and pethidine (50 mg). Their cardiorespiratory functions were monitored continuously during the procedure. All APCs were performed by experienced gastrointestinal endoscopists (J.Y.A., H.K.N., K.W.J., J.H.L., D.H.K., K.D.C., H.J.S., G.H.L., and H.Y.J.) using a single-channel endoscope (GIF-H260 or GIF-HQ290; Olympus Optical Co. Ltd, Tokyo, Japan). For APC (APC 300; Erbe Electromedicine, Tübingen, Germany), after confirming the lesion, saline containing epinephrine (0.01 mg/mL) and indigo carmine was submucosally injected using a 23-gauge needle, and the lesion was ablated using APC. The gas flow rate was 1.8 L/min, and the electrical current was set at either 60 or 80 W.

3. Follow-up schedule

All patients were hospitalized on the day of the procedure and underwent blood tests including complete blood count (CBC), electrolyte battery, coagulation battery (activated partial thromboplastin time and prothrombin time), chemical battery, and chest X-ray. CBC, chest radiography, and conventional endoscopy were also performed on the next day (second-look endoscopy) after the procedure to assess for postprocedural complications. If no bleeding appeared upon second-look endoscopy, oral diet and an order for discharge could be possible on that day. A proton-pump inhibitor (pantoprazole 40 mg) was intravenously administered from the morning on the procedure day until the nothing-by-mouth period, followed by oral proton-pump inhibitor therapy for 4 to 8 weeks.

All patients visited the outpatient clinic for their first follow-up at 2 weeks after discharge; they underwent a CBC test and were checked for the occurrence of complications. One hospital coordinator (a specialized nurse) managed all patients and conducted follow-up surveys on

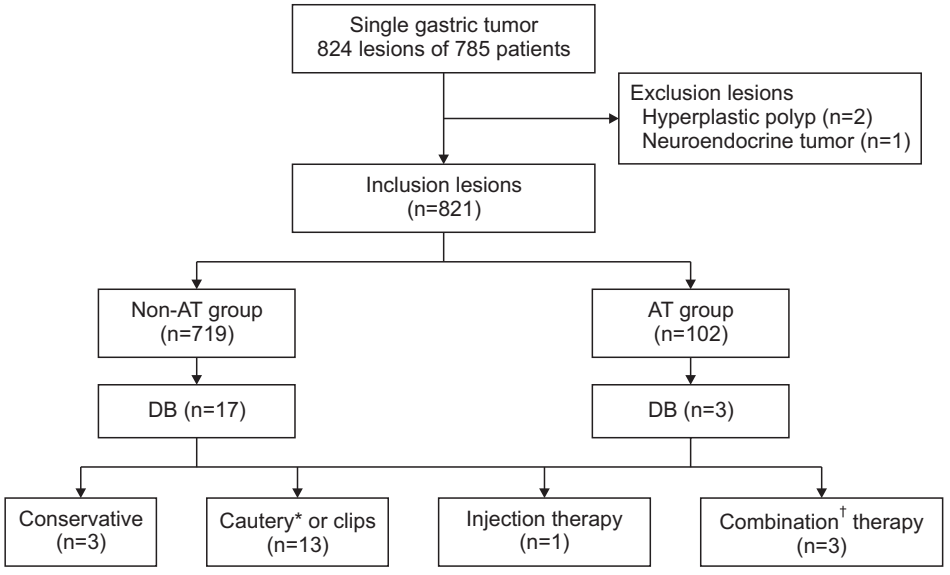

Fig. 1. Patient inclusion and management flow.
AT, antithrombotics; DB, delayed bleeding. *Cautery devices include argon plasma coagulation and electrocautery probes; †Combination therapy is the use of injection therapy in conjunction with a second endoscopic treatment modality such as cautery or clips.

the incidence of DB and thromboembolic events (TEs) through phone counseling from the first outpatient clinic visit (before admission) to 1 month after the procedure.

4. Definition

Antithrombotic agents were classified as anticoagulants (ACs) or antiplatelet agents (APs). APs include aspirin, thienopyridines (prasugrel, clopidogrel, ticagrelor, and ticlopidine), and other platelet aggregation inhibitors (cilostazol, triflusal, limaprost, and sarpogrelate). We excluded the glycoprotein IIb/IIIa receptor inhibitors and the protease-activated receptor-1 inhibitor vorapaxar because no patients used these antithrombotic agents. We also excluded nonsteroidal anti-inflammatory drugs because of their variable half-life and types. ACs include the following four drug classes: vitamin K antagonists (warfarin), heparin derivatives (unfractionated and low molecular weight, fondaparinux), direct thrombin inhibitors (hirudin, dabigatran, and argatroban), and direct factor Xa inhibitors (apixaban, rivaroxaban, and edoxaban).

According to the timing of antithrombotic agent cessation, the antithrombotics (AT) group was subdivided into the following three groups: a continuation group, a regular cessation group, and a prolonged cessation group. In the continuation group, the patients received antithrombotic therapy until the day of gastric APC or stopped receiving antithrombotic therapy 0–4 days prior to gastric APC. In the regular cessation group, the patients stopped receiving antithrombotic therapy 5–7 days prior to gastric APC. In the prolonged cessation group, the patients stopped receiving antithrombotic therapy 8–14 days prior to gastric APC.

Resuming antithrombotic therapy was decided at the discretion of the attending physicians, with the consultation of a cardiologist or neurologist if necessary.

DB was defined as presenting when the patient showed obvious hematemesis, hematochezia, or melena regardless of whether additional endoscopy was performed, or revealed a hemoglobin level decrease of ≥2 g/dL with bleeding stigmata on additional endoscopy. Especially, after discharge, if a patient complained of dizziness, general weakness, and nausea or vomiting during the phone counseling with the coordinator, the patient was required to visit the outpatient clinic for a consultation with the physician and a CBC test. Additionally, patients with a hemoglobin level decrease of ≥2 g/dL on CBC test had to undergo additional endoscopy to find the bleeding stigmata.

According to the timing of bleeding, early DB (EDB) was defined as hematemesis, hematochezia, or melena occurring from the end of APC to second-look endoscopy or as active or possible bleeding at the time of the second-look endoscopy, such as Forrest classifications Ia, Ib, and IIa. Late DB (LDB) was defined as hematemesis, hematochezia, melena, or decreased hemoglobin (≥2 g/dL) between the period of the second-look endoscopy and 1 month after the procedure.[13,14]

TEs (cerebral infarction, transient ischemic attack, acute myocardial infarction, pulmonary embolism, or deep vein thrombosis) were monitored from the first day of discontinuation of antithrombotic agents to 30 days after APC.[15]

5. Outcome measures

The outcome measures were as follows: (1) DB rate in non-AT and AT groups, (2) DB rate according to the cessation status of antithrombotic agents, (3) TE rate in AT group, and (4) the risk evaluation of various clinical factors affecting DB.

6. Statistical analysis

To compare the DB rate between non-AT and AT groups, categorical data were compared using the chi-square test and the Fisher exact test and continuous data were compared by the Student t-test or the Mann-Whitney U test.

To identify important risk factors for DB after APC, we performed a univariate and multivariate logistic regression analysis. For the univariate analyses, the categorical variables were compared using the chi-squared test and the Fisher exact test, and those variables with p-values <0.05 were included in the multivariate analyses. The odds ratios (ORs) and 95% confidential intervals (CIs) were calculated using logistic regression analyses to identify the factors associated with post-APC bleeding. A value of $p<0.05$ were considered statistically significant. All of the statistical analyses were performed using IBM SPSS Statistics version 23.0 for Windows (IBM Corp., Armonk, NY, USA).

RESULTS

1. Baseline characteristics

The baseline clinicopathologic characteristics of the patients are shown in Table 1. The mean tumor size was 9.1 mm (standard deviation, 5.3 mm) and the largest size was 60 mm. Liver cirrhosis was found in 16 cases (1.9%) and all of them had mild liver dysfunction, classified as a Child-Turcotte-Pugh score A. Histologically, among 762 cases (92.8%) of adenoma, low-grade and high-grade dysplasia was found in 698 (85.0%) and 64 cases (7.8%), respectively. In 59 cases (7.2%) with early gastric cancer, 51 cases (6.2%) were diagnosed as well or moderately differentiated adenocarcinoma and eight cases (1.0%) were identified as poorly differentiated adenocarcinoma or signet ring cell carcino-

Table 1. Clinicopathologic Characteristics of Patients Not Receiving Antithrombotic and Receiving Antithrombotic Therapy

Characteristics	Total (n=821)	Non-AT group (n=719)	AT group (n=102)	p-value
Sex				0.006
Female	241 (29.4)	223 (31.0)	18 (17.6)	
Male	580 (70.6)	496 (69.0)	84 (82.4)	
Age, yr	65.3±9.8	64.5±9.8	70.4±8.2	<0.001
LC				0.708
No	805 (98.1)	704 (97.9)	101 (99.0)	
Yes*	16 (1.9)	15 (2.1)	1 (1.0)	
CKD				<0.001
No	765 (93.2)	679 (94.4)	86 (84.3)	
Yes†	56 (6.8)	40 (5.6)	16 (15.7)	
Diagnosis				0.274
Adenoma	762 (92.8)	670 (93.2)	92 (90.2)	
EGC	59 (7.2)	49 (6.8)	10 (9.8)	
Tumor size, mm	9.1±5.3	9.0±5.1	9.8±6.3	0.115
Location				0.549
Lower third	333 (40.6)	292 (40.6)	41 (40.2)	
Middle third	326 (39.7)	289 (40.2)	37 (36.3)	
Upper third	162 (19.7)	138 (19.2)	24 (23.5)	

Data are presented as number (%) or mean±SD.
AT, antithrombotics; LC, liver cirrhosis; CKD, chronic kidney disease; EGC, early gastric cancer.
*All of the patients with LC had mild liver dysfunction, classified as Child-Turcotte-Pugh score A; †None of the patients with CKD underwent dialysis.

Table 2. Comparison of Clinical Outcomes in the Non-AT Group and the AT Group

Outcome	Total (n=821)	Non-AT group (n=719)	AT group				p-value (non-AT vs AT)	p-value (non-AT vs CG)	p-value (non-AT vs RCG)	p-value (non-AT vs PCG)
			All (n=102)	CG (n=16)	RCG (n=47)	PCG (n=39)				
Days of hospitalization	3.0 (2.0–3.0)	3.0 (2.0–3.0)	3.0 (2.0–3.0)	3.5 (2.3–4.0)	2.0 (2.0–3.0)	3.0 (2.0–4.0)	-	-	-	-
DB	20 (2.4)	17 (2.4)	3 (2.9)	2 (12.5)	1 (2.1)	0	0.728	0.061	>0.999	>0.999
EDB	7 (0.9)	6 (0.8)	1 (1.0)	1 (6.3)	0	0	>0.999	0.143	>0.999	>0.999
LDB	13 (1.6)	11 (1.5)	2 (2.0)	1 (6.3)	1 (2.1)	0	0.670	0.234	0.535	>0.999

Data are presented as median (IQR) or number (%).
AT, antithrombotics; CG, continuation group; RCG, regular cessation group; PCG, prolonged cessation group; DB, delayed bleeding; EDB, early delayed bleeding; LDB, late delayed bleeding; IQR, interquartile range.

ma. Many of the tumors were located in the lower (40.6%) or middle third (39.7%) of the stomach. However, compared with the cases without antithrombotic therapy, cases with antithrombotic therapy were significantly more likely to include older male patients (69.0% vs 82.4%, p=0.006; mean age 64.5 years vs 70.4 years, p<0.001). Of 56 patients with chronic kidney disease (CKD) who were confirmed glomerular filtration rate less than 60 mL/min/1.73 m^2 in the laboratory test, none of them received dialysis and the proportion of CKD was significantly larger in the AT group than the non-AT group (15.7% vs 5.6%, p<0.001).

2. Clinical outcomes

Table 2 and Fig. 2 show the incidence of procedure-related complications in the non-AT and AT groups. The median days of hospitalization were 3.0 days (interquartile

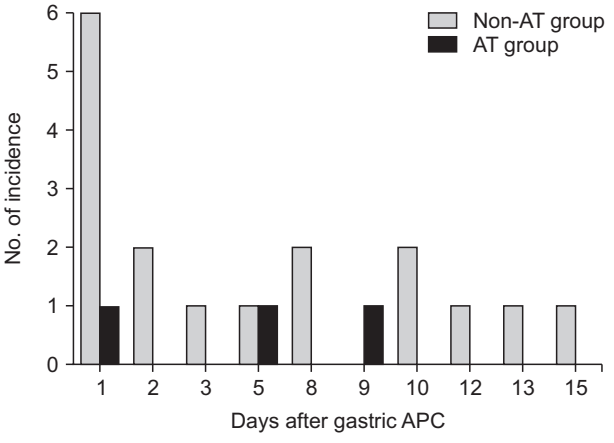

Fig. 2. The day of delayed bleeding after gastric APC.
APC, argon plasma coagulation; AT, antithrombotics.

range, 2.0 to 3.0 days) and there were no cases with procedure-related perforation or TE within 30 days.

Among all the cases, those receiving antithrombotic therapy did not have a significantly higher incidence of DB than those not receiving antithrombotic therapy (2.9% [3/102] vs 2.4% [17/719], p=0.728). Additionally, both the EDB and LDB rate did not significantly differ between the non-AT and AT groups (0.8% [6/719] vs 1.0% [1/102], p>0.999; 1.5% [11/719] vs 2.0% [2/102], p=0.670).

According to the analysis of the antithrombotics cessation timing, the continuation group showed a higher bleeding tendency than the non-AT group; however, the difference was not significant (12.5% [2/16] vs 2.4% [17/719], p=0.061). There were no differences in the DB rates of the regular cessation and prolonged cessation groups in comparison with the non-AT group.

3. The incidence of EDB and LDB depending on the type of antithrombotic agents

Table 3 shows the EDB and LDB rates according to the types of antithrombotic agents and considering the cessation timing of the drug. Of 102 patients receiving antithrombotic therapy, there were 56 patients taking aspirin, 22 taking other AP except for aspirin, 13 taking AC, and 11 taking two or more antithrombotic agents. There were no patients with DB in both the aspirin group and AC group. Among 22 other AP users, one patient (4.5%) experienced LDB. In the combination group, one patient each presented EDB (9.1%) and LDB (9.1%), respectively.

4. Risk factors of DB after gastric APC

Table 4 shows the analysis of potential risk factors causing DB. Univariate analysis revealed significant risk factors: male (OR, 8.13; 95% CI, 1.08 to 61.10; p=0.042), CKD (OR, 4.90; 95% CI, 1.71 to 14.02; p=0.003), tumor in upper third of stomach (OR, 3.41; 95% CI, 1.10 to 10.59; p=0.034), and continued antithrombotic therapy (OR, 5.90; 95% CI, 1.24 to 28.01; p=0.026). Multivariate analysis confirmed significant independent risk factors: male sex (OR, 7.66; 95% CI, 1.02 to 57.69; p=0.048) and CKD (OR, 4.51; 95% CI, 1.57 to 13.02; p=0.005).

5. Management in patients with DB

Fig. 1 presents the management flow in the cases with the occurrence of DB after gastric APC. Among 20 cases with DB, there were three cases receiving conservative management, 13 cases treated with additional APC, hemostatic forceps, or endoscopic clips, one case undergoing injection therapy, and three cases receiving combination treatment. Blood transfusion was needed in four patients (20.0%) and their mean number of transfused red blood cells was 2.3 units. All of the patients achieved successful hemostasis and no one underwent additional serious complication.

DISCUSSION

APC has been used to treat a broad range of gastrointestinal problems, including bleeding ulcers,[16] Dieulafoy's lesions,[17] angiodysplasia,[8,18] and tumors.[6,19] According to previous studies, APC is an effective and safe treatment option for gastric neoplasms.[4-6] Despite this safety, as the widening applications of gastric APC, complications such as hemorrhage and perforation have often been reported.[6,20,21] While many studies of risk factors for DB have been reported in gastric ESD, there have been no studies about risk factors for post-APC bleeding.

Table 3. The Incidence of EDB and LDB Depending on the Type of Antithrombotic Agents

Variable	Aspirin group	Other AP group*	AC group	Combination group†
Continuation group	3 Lesions	3 Lesions	7 Lesions	3 Lesions
EDB	0	0	0	1 (33.3)
LDB	0	0	0	1 (33.3)
Regular cessation group	24 Lesions	11 Lesions	6 Lesions	6 Lesions
EDB	0	0	0	0
LDB	0	1 (9.1)	0	0
Prolonged cessation group	29 Lesions	8 Lesions	0 Lesions	2 Lesions
EDB	0	0	-	0
LDB	0	0	-	0
Total	56 Lesions	22 Lesions	13 Lesions	11 Lesions
EDB	0	0	0	1 (9.1)
LDB	0	1 (4.5)	0	1 (9.1)

Data are presented as number (%).
EDB, early delayed bleeding; LDB, late delayed bleeding; AP, antiplatelet agent; AC, anticoagulant.
*Other AP group included other antiplatelet agent users except for those using aspirin; †Combination group included the patients taking two or more antithrombotic agents.

Table 4. The Risk Factors for DB after Gastric Argon Plasma Coagulation

Factor	Non-DB (n=801)	DB (n=20)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	p-value	OR (95% CI)	p-value
Sex						
Female	240 (30.0)	1 (5.0)	1		1	
Male	561 (70.0)	19 (95.0)	8.13 (1.08–61.10)	0.042	7.66 (1.02–57.69)	0.048
Age, yr	65.2±9.8	66.3±9.5	1.01 (0.97–1.06)	0.647		
LC						
No	785 (98.0)	20 (100)	1			
Yes*	16 (2.0)	0	NA	NA		
CKD						
No	750 (93.6)	15 (75.0)	1		1	
Yes†	51 (6.4)	5 (25.0)	4.90 (1.71–14.02)	0.003	4.51 (1.57–13.02)	0.005
Diagnosis						
Adenoma	745 (93.0)	17 (85.0)	1			
EGC	56 (7.0)	3 (15.0)	2.35 (0.67–8.25)	0.183		
Tumor size, mm	9.1±5.3	9.9±2.8	1.02 (0.96–1.09)	0.505		
Location						
Lower third	328 (40.9)	5 (25.0)	1		1	
Middle third	319 (39.8)	7 (35.0)	1.44 (0.45–4.58)	0.537	1.25 (0.38–4.05)	0.714
Upper third	154 (19.2)	8 (40.0)	3.41 (1.10–10.59)	0.034	2.85 (0.88–9.18)	0.080
Antithrombotic therapy						
No	702 (87.6)	17 (85.0)	1		1	
Continuation	14 (1.7)	2 (10.0)	5.90 (1.24–28.01)	0.026	3.31 (0.57–19.32)	0.183
Regular cessation	46 (5.7)	1 (5.0)	0.90 (0.12–6.90)	0.917	0.56 (0.07–4.54)	0.583
Prolonged cessation	39 (4.9)	0	NA	NA	NA	NA

Data are presented as number (%) or mean±SD.

DB, delayed bleeding; OR, odds ratio; CI, confidential interval; LC, liver cirrhosis; CKD, chronic kidney disease; EGC, early gastric cancer; NA, not available.

*All of the patients with LC had mild liver dysfunction, classified as Child-Turcotte-Pugh score A; †None of the patients with CKD underwent dialysis.

Especially with the advance of an aging society, we have an increasing opportunity to carry out therapeutic endoscopy among elderly and comorbid patients receiving antithrombotic therapy.[22,23] Thus, we carried out the study of patients receiving antithrombotic agents to identify DB risk and determine the proper timing of drug cessation in gastric APC.

In our study, the DB rate of the AT group was not significantly different from the non-AT group (2.9% vs 2.4%, p=0.728) and a TE was not observed in all patients taking antithrombotic agents.

In baseline characteristics, the AT group had more elderly male participants and high proportion of CKD than the non-AT group (male 82.4% vs 69.0%, p=0.006; mean age 70.4 years vs 64.5 years, p<0.001; CKD 15.7% vs 5.6%, p<0.001). We believed that is because the patients receiving antithrombotic therapy tended to have diseases with a greater incidence in elderly populations, such as diabetes, cardio- and cerebrovascular disease. Despite these differences, we tried to compare the incidence of gastric APC complications objectively in the AT and non-AT groups by identifying the proper distribution of the lesion's features including diagnosis, size, and location.

Our study showed that antithrombotic therapy within 2 weeks of gastric APC did not increase bleeding tendency. However, we also wanted to know the DB rate according to the cessation timing of antithrombotic agents.

Consequently, we found that there were no patients with DB in the prolonged cessation group and only one patient with DB in the regular cessation group, but they did not show significant differences in bleeding rate compared with the non-AT group (2.1% vs 2.4%, p>0.999). The continuation group showed a higher, but not significant, bleeding tendency than the non-AT group (12.5% [2/16] vs 2.4% [17/719], p=0.061). However, this result from the continuation group might be due to an insufficient number of patients, and further studies are needed.

In addition, we compared the DB rate by categorizing antithrombotic users into the aspirin group, other AP group, AC group, and combination group. Even though it was impossible to apply statistical analysis because of the small number of patients of each group, we found that the DB did not occur in aspirin or AC users in contrast to the AP and combination groups. However, to identify the ef-

fect of each antithrombotic agent, we need more detailed studies in the future with a larger number of patients.

As the development and use of ESD have increased, many studies have assessed the risk factors for bleeding after gastric ESD. Several previous studies have reported that the risk factors of post-ESD bleeding are age, sex, tumor location, the size of the resected specimen, diagnosis, CKD, liver cirrhosis, and the use of antithrombotic agents.[24-27] However, unlike ESD, there has been no study focusing on the risk factors of post-APC bleeding.

As the first study focusing on risk factors of post-APC bleeding, we found that male sex and CKD were significant and independent risk factors in the multivariate analysis; however, contrary to the results of the univariate analysis, continued antithrombotic therapy was not a meaningful risk factor of DB in multivariate analysis. While many studies[24,27,28] reported that antithrombotic therapy clearly increased the risk of post-ESD bleeding, our result showed that the use of antithrombotic agents did not have significant effect on occurrence of DB in APC, which is a low-risk procedure. Therefore, we thought that gastric APC can be performed with relative safety even in patients with a high thromboembolic risk requiring continued antithrombotic therapy. APC could be an alternative treatment option in selected patients. However, ESD should be considered preferentially for treating gastric neoplasms, because it can provide accurate histological diagnosis for confirming curative resection.

Several studies reported that CKD is a major risk factor for post-ESD bleeding, especially in hemodialysis.[24,29] Libânio *et al.*[24] in their systematic review and meta-analysis showed that CKD could increase bleeding risk 3.38 times after ESD (OR, 3.38; 95% CI, 2.31 to 4.97). Corresponding to these ESD results, our study found that CKD was a risk factor for post-APC bleeding (OR, 4.51; 95% CI, 1.57 to 13.02; p=0.005). Interestingly, none of the CKD patients in our study were undergoing dialysis; however, we thought that if there were patients undergoing dialysis, the bleeding risk of those patients might be higher than those who were not. Thus, in the future, it is necessary to analyze the post-APC bleeding risk according to the stage of CKD.

In patients taking antithrombotic agents, TE is one of the fatal complications that could occur before and after endoscopic procedures. In our study, TE was not observed within 30 days after endoscopic resection. This result might be affected by the retrospective study design, and we tried to minimize the interruption of antithrombotic agents by consulting with a cardiologist or a neurologist in the case of high thromboembolic risk. However, because the evaluation period of the TE may not be long enough to adequately analyze the event, we should not overlook the risk of TE.

This study has several limitations. First, this retrospective study had a selection bias. In order to overcome this bias and identify the effect of antithrombotic therapy clearly, we tried to perform propensity score matching. However, the sample size of case group and event outcomes were not enough to apply the matching. Second, we could not evaluate the effect of DB depending on the timing of antithrombotic agent resumption. Third, the baseline characteristics differed between the non-AT and AT groups in several factors. Finally, our study could not reflect other risk factors such as genetic predisposition, other comorbidities, and some medications or supplements affecting platelet function. Nevertheless, this study has the advantage of being a first study that proves the DB rate after gastric APC depending on the antithrombotic therapy.

In conclusion, antithrombotic therapy is acceptably safe in gastric APC, because it does not significantly increase the incidence of DB. Although gastric APC has a relatively lower incidence of DB, patients with CKD or male sex require a careful follow-up survey on the incidence of post-APC bleeding.

CONFLICTS OF INTEREST

J.Y.A. is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

AUTHOR CONTRIBUTIONS

Study concept and design: J.Y.A. Data acquisition: J.Y.A., H.K.N., K.W.J., J.H.L., D.H.K., K.D.C., H.J.S., G.H.L., H.Y.J. Data analysis and interpretation: S.S., J.H.N., J.Y.A. Statistical analysis: S.S., J.H.N. Study supervision: J.Y.A. Drafting of the manuscript: S.S., J.H.N. Writing - review & editing: S.S., J.H.N., J.Y.A. Approval of final manuscript: all authors.

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