Journal of Gastroenterology and Hepatology

JGHF

doi:10.1111/jgh.16004

ORIGINAL ARTICLE - ENDOSCOPY

Efficacy analysis of hemostatic spray following endoscopic papillectomy: A multicenter comparative study

Kyong Joo Lee,* Tae Hoon Lee,† Jae Hee Cho,‡ Jong Jin Hyun,§ Sung Ill Jang,‡ Seok Jeong,¶ Jin-Seok Park,¶ Jae Kook Yang,† Don Haeng Lee,¶ Dong Ki Lee‡ and Sang Heum Park†

*Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, †Division of Gastroenterology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan, ‡Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, §Department of Internal Medicine, Korea University College of Medicine, Seoul, ¶Department of Internal Medicine, Inha University College of Medicine, Incheon, Korea

Key words
bleeding, delayed bleeding rate, endoscopic papillectomy, hemostatic spray, prophylaxis.

Accepted for publication 17 September 2022.

Correspondence
Dr Tae Hoon Lee, Division of Gastroenterology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Cheonan Hospital, 31, Soonchunhyang 6-gil, Dongnamgu, Cheonan-si, Chungcheongnam-do 31151, Republic of Korea.
Email: thlee9@schmc.ac.kr

Declaration of conflict of interest: The authors have no conflicts of interest to declare for this article.

Author contribution: T.H.L. conceived and designed the study. K.J.L., T.H.L., J.H.C., J.J.H., S.I.J., S.J., J.S.P., J.K.Y., D.H.L., D.K.L., and S.H.P. contributed to the data collection and analyses. K.J.L. and T.H.L. drafted the manuscript, and all authors read and approved its final version.

Ethical approval: This study was performed in compliance with the principles of the Declaration of Helsinki and was approved by Human Ethics Review Committee of each hospital. Written informed consent for this study was waived by the ethics committee due to its retrospective design.

Abstract

Background and Aim: Endoscopic post-papillectomy bleeding is a serious adverse event with a prevalence ranging from 2% to 45.3%. Conventional hemostatic methods, including diluted epinephrine injection before papillectomy or argon plasma coagulation after papillectomy, did not show a preventive role in reducing immediate or delayed post-papillectomy bleeding. Therefore, we aimed to assess the efficacy and safety of a hemostatic powder spray for post-papillectomy bleeding and compare with those of conventional modalities.

Methods: Patients who underwent endoscopic papillectomy were enrolled in five tertiary hospitals. The group was divided into hemostatic spray and conventional control groups according to the bleeding control methods. The main outcome measurements were delayed bleeding rate and any adverse events related to the procedures.

Results: A total of 40 patients who received a hemostatic spray (n = 18) or conventional hemostatic methods (n = 22) after endoscopic papillectomy were included. The prevalence of delayed bleeding was not different in the two groups: 27.8% and 36.4% in hemostatic spray and conventional control groups (P = 0.564), respectively. The adverse events such as post-papillectomy pancreatitis and cholangitis were not different in the two groups. There were no procedure-related mortalities.

Conclusion: Hemostatic spray is technically feasible and safe for the prevention or management of post-papillectomy bleeding. Hemostatic spray can be one of the options for post-papillectomy bleeding control methods owing to its convenient use.

Financial support: This research was supported by the Soonchunhyang University Research Fund and a grant from the Patient-Centered Clinical Research Coordinating Center (PACEN), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HC21C0016000021). Nexpowder and hemostatic powder were provided by NextBiomedical (Incheon, Republic of Korea). The funder/sponsor had no role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Introduction

Although endoscopic papillectomy (EP) using a snare is now considered a safe and effective treatment option for ampullary adenoma, the risk of EP-related adverse events is not negligible.[1,2] In particular, pancreatitis (3–33%) and bleeding (2–45.3%) are the most common and troublesome adverse events following EP.[3–6] Several studies have recommended placement of a pancreatic duct stent after EP to reduce the severity or frequency of pancreatitis.[1–3,7,8] In addition to the placement of a pancreatic duct stent, rectal nonsteroidal anti-inflammatory drugs are recommended to further prevent pancreatitis after EP.[1] This recommendation is supported by prior studies investigating the prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis.[9,10]

However, there is a lack of data how to prevent immediate or delayed bleeding after EP, and a method of prophylactic

hemostasis has not yet been established. Angiographic embolization or surgery is considered in cases of massive bleeding that are unresponsive to endoscopic therapy; however, this has been associated with increased morbidity and mortality rates. Several studies have evaluated the role of adjunctive argon plasma coagulation (APC) after EP.[11,12] The results were conflicting, with only some indicating that APC was effective at preventing delayed post-EP bleeding. Preventive closure of the frenulum by clipping after EP was found to be effective for the prevention of delayed bleeding, but the number is too small to generalize in clinical practice.[13] Recently, a rotatable clip showed protective effect for delayed EP bleeding; however, it did not show any statistical significance when compared with that in the non-clipping group, and the prevalence of pancreatitis was relatively high in the clipping group without statistical significance.[14] Submucosal injection of diluted epinephrine before EP did not prevent delayed post-EP bleeding compared with simple snare papillectomy.[15]

Recently, as an another emerging method, the application of hemostatic spray powder was proven to be effective for non-variceal upper gastrointestinal bleeding (UGIB).[16,17] Nexpowder (UI-EWD, Nextbiomedical, Incheon, Republic of Korea) was also introduced as an effective method to allow bleeding control in upper gastrointestinal bleeding. The advantage of Nexpowder is that it has stronger adhesion leading to less catheter clogging while delivering to the sites of bleeding.[18] Hemostatic spray powder is recommended for patients with active bleeding ulcers in the American College of Gastroenterology clinical guideline[19] and the European Society of Gastrointestinal Endoscopy guideline[20]; however, evidence for their efficacy in post-EP bleeding is lacking.

Therefore, this study aimed to evaluate the efficacy and safety of hemostatic spray powder in preventing post-EP bleeding and immediate bleeding control.

Methods

Patients. Patients underwent EP between June 2019 and December 2021 in five tertiary hospitals were prospectively included and retrospectively analyzed with control group. According to the bleeding control methods, the patients were divided into two groups: hemostatic spray and conventional control groups. Biopsy pathologies were confirmed before EP, and ampullary adenomas or neuroendocrine tumors were included. To prevent delayed bleeding, patients who received either hemostatic spray or conventional control methods for prophylactic hemostasis or immediate bleeding control were included. Patients with liver cirrhosis or chronic renal failure with a high bleeding tendency were excluded. In the case of taking anticoagulants, it was stopped 5 to 7 days before EP. This study was performed in compliance with the principles of the Declaration of Helsinki and was approved by the Institutional Review Board of each hospital. The need for informed consent was waived due to the retrospective nature of the study.

Endoscopic procedure. Conventional snaring, with or without submucosal diluted epinephrine injection, was performed for EP. After papillectomy, insertion of the biliary stent and pancreatic duct stent was attempted. In hemostatic spray group, Nexpowder (UI-EWD, Nextbiomedical, Incheon, Republic of Korea) was applied to the resected lesions for the prophylaxis of delayed bleeding (Video S1), to control immediate bleeding (Video S2 and Fig. 1), or additional bleeding control following other conventional methods (Video S3). Nexpowder was applied through the endoscopic working channel using an 8 Fr catheter and spraying device under direct endoscopic vision. After positioning the catheter for powder delivery, the working endoscopic channel was flushed with air (delivered using a 60 mL syringe) to ensure that the catheter tip was dry. Initially, 3 g of UI-EWD was administered to the bleeding lesion. If bleeding was not controlled, Nexpowder administration was repeated up to a maximum powder delivery of 6 g. In the conventional control group, diluted epinephrine injection, APC, and hemoclip were used for prophylactic hemostasis or immediate bleeding control. Conventional control methods were also used in hemostatic spray group adjunct to the hemostatic spray as needed. Endoscopy was performed the next day within 24 h, and endoscopy was performed if there was a hemodynamic change within 1 week.

Definition of adverse events. The primary endpoint of this study was the rate of delayed post-EP bleeding in both groups. Bleeding was defined as a drop in hemoglobin level of more than 3 g/dL, the requirement of transfusion, or clinical indications of bleeding (hematemesis and melena). Delayed bleeding was defined as bleeding from the resected lesion after 12–24 h by clinical

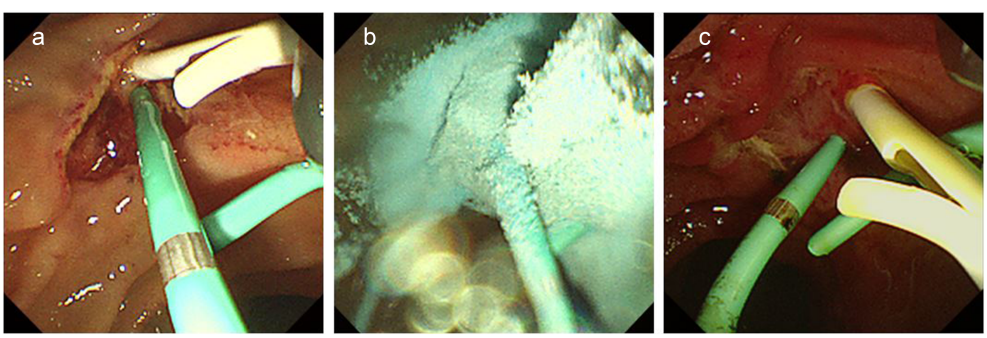

Figure 1 Application of the hemostatic spray. (a) The biliary stent and pancreatic duct stent were inserted after endoscopic papillectomy and there was an immediate minor bleeding from the resected lesion. (b) Hemostatic spray was applied to the resected lesion to control immediate bleeding. (c) Endoscopic findings the day after endoscopic papillectomy showed that the hemostatic spray was eliminated spontaneously and there was no active bleeding.

manifestations or endoscopic finding. Endoscopic hemostasis was performed if there was any evidence of bleeding. The secondary endpoint was any adverse events, including pancreatitis, cholangitis, perforation, embolization, surgery, and mortality within 7 days of treatment. Post-EP pancreatitis was characterized as pancreatic abdominal pain occurring within 24 h of the procedure and elevation of serum amylase levels at least three times above normal.[21] Asymptomatic hyperamylasemia after EP was defined as a serum amylase levels increased three times or more than upper normal limit in the first 24 h without abdominal pain.

Statistical analysis. Categorical variables were presented as frequency and percentage whereas continuous variables as mean (± standard deviation). Paired *t*-testing was used to compare continuous variables, and the χ^2 test was used to compare categorical variables between hemostatic spray and conventional control groups. The odds ratios (ORs) and confidence intervals (CIs) for developing of delayed bleeding were calculated using multivariable logistic regression analyses after adjustment for confounding variables. Statistical analyses were performed using SPSS 25 (IBM SPSS Statistics for Mac, Armonk, NY, IBM Corp). *P* values of < 0.05 were considered statistically significant.

Results

Baseline characteristics. A total of 40 patients were enrolled in this study, and the baseline patient characteristics have been described in Table 1. The patients were divided into hemostatic spray (n = 18) and conventional control groups (n = 22) according to the bleeding control methods. The baseline characteristics including sex, age, comorbidities, and the use of antiplatelets were similar in the two groups. The number of high-grade dysplasia adenoma was relatively higher in the conventional control group without statistical significance.

Clinical outcomes. In the hemostatic spray group, 11 patients who did not develop immediate bleeding after EP underwent hemostatic spray only for the prophylaxis of delayed bleeding (Fig. 2). Other seven patients either underwent hemostatic spraying alone or hemostatic spraying after other hemostatic methods such as hemoclips or APC. In the conventional control group, prophylactic hemostasis after EP was performed by conventional APC, diluted epinephrine injection, or hemoclips as well as immediate bleeding control (Fig. 2). Most of the patients received en-bloc resection in the two groups. The number of patients who received a biliary stent was significantly more in the

Table 1 Baseline characteristics and clinical outcomes of the study participants

Variables, *n* (%)	Total (n = 40)	Hemostatic spray group (n = 18)	Conventional control group (n = 22)	*P*-value
Sex				0.324
Male	21 (52.5)	11 (61.1)	10 (45.5)	
Female	19 (47.5)	7 (38.9)	12 (54.5)	
Age, years, mean ± SD	60.2 ± 11.6	60.7 ± 12.8	59.8 ± 10.7	0.808
Comorbidities				
Hypertension	17 (42.5)	10 (55.6)	7 (31.8)	0.131
Diabetes mellitus	7 (17.5)	2 (11.1)	5 (22.7)	0.336
Medications				
Antiplatelets	6 (15)	2 (11.1)	4 (18.2)	0.533
Biopsy pathology				0.109
Adenoma, low-grade dysplasia	32 (80)	15 (83.3)	17 (77.3)	
Adenoma, high-grade dysplasia	6 (15)	1 (5.6)	5 (22.7)	
Neuroendocrine tumor	2 (5)	2 (11.1)	0	
Resection method				0.884
En-bloc resection	38 (95)	17 (94.4)	21 (95.5)	
Piecemeal resection	2 (5)	1 (5.6)	1 (4.5)	
Pancreatic duct stent	36 (90)	18 (100)	18 (81.8)	0.057
Biliary stent	24 (60)	17 (94.4)	7 (31.8)	<0.001
Diluted epinephrine injection before EP	16 (40)	8 (44.4)	8 (36.4)	0.604
Purpose of hemostasis after EP				0.324
Prophylactic aim	17 (42.5)	11 (61.1)	10 (45.5)	
Immediate hemostasis	23 (57.5)	6 (27.3)	12 (54.5)	
Tumor size, mm, mean ± SD	11.7 ± 3.9	12.3 ± 4.6	11.1 ± 3.2	0.365
Final pathology				0.175
Adenoma, low-grade dysplasia	29 (72.5)	13 (72.2)	16 (72.7)	
Adenoma, high-grade dysplasia	6 (15)	1 (5.6)	5 (22.7)	
Adenocarcinoma	3 (7.5)	2 (11.1)	1 (4.5)	
Neuroendocrine tumor	2 (5)	2 (11.1)	0	
Total procedure time, minutes, mean ± SD	23.0 ± 8.4	24.6 ± 5.9	21.6 ± 9.9	0.265

SD, standard deviation; EP, endoscopic papillectomy.

hemostatic spray group than in the conventional control group (94.4% *vs* 31.8%). The tumor size, types of final pathology, and total procedure time were not different between the two groups (Table 1).

Analysis of adverse events according to the bleeding control methods. Adverse events have been described in Table 2. As a primary outcome, delayed bleeding was developed in 5 (27.8%) and 8 (36.4%) patients in the hemostatic spray group *versus* the conventional control group ($P = 0.564$), respectively. In hemostatic spray group, the delayed bleeding rate was 18.1% (2/11) in the prophylactic hemostasis group and 42.8% (3/7) in the immediate bleeding control group. Whereas, in the conventional control group, the delayed bleeding rates were 20% (2/10) in prophylactic hemostasis group and 50% (6/12) in immediate bleeding control group (Fig. 2). The symptoms such as melena or hematemesis were not different and there was no patient who required transfusion. The hemoglobin change before and after EP was similar in the two groups.

The number of asymptomatic hyperamylasemia and post-EP pancreatitis was not different in the two groups. No other serious adverse events or mortalities occurred in both groups. Regarding predictive factors of delayed bleeding after EP, the bleeding control methods were not significantly related with the predictive factor of delayed bleeding (hemostatic spray group, OR 1.23, 95% CI 0.21–7.12) (Table 3).

Discussion

Our clinical study is the first to show the technical and clinical feasibility of using hemostatic spray powder for the management of immediate bleeding control and prevention of delayed post-EP bleeding. The success rate of bleeding control was similar to that in the conventional control group. Hemostatic spray has the advantage of being technically easy to use and safe. The rate of reported adverse events was acceptable compared with previous reports,[11,12,15,22] and no cases of morbidity or mortality occurred after hemostatic spray use.

EP is a relatively safe endoscopic procedure that can replace surgery in cases of ampullary adenomas. However, immediate and delayed bleeding are lethal complications of EP. Generally, the methods of endoscopic hemostasis for post-sphincterotomy bleeding or post-EP bleeding are similar to those used for UGIB. Similar to EP procedures, endoscopic mucosal resection or endoscopic submucosal dissection also carry the risk of delayed bleeding as a major adverse event. Coagulation of exposed non-bleeding visible vessels and the use of a hemostatic clip are relatively easy and convenient with forward-viewing endoscopes.[23] However, it is technically challenging to use a hemostatic clip or thermal device with side-viewing endoscopes because of the tangential approach.[24] Also, there are anatomical differences such as pancreatic and bile duct openings, and blockage of openings should be prevented prior to treatment. Conventional bleeding control techniques, such as the application of hemoclip, APC, fibrin glue, or diluted epinephrine injection, may cause ductal obstruction and trauma, resulting in serious adverse events such as pancreatitis, cholangitis, or stricture. Previous studies have evaluated the efficacy of diluted epinephrine injection and prophylactic APC for the prevention of delayed EP bleeding, but the results were not promising.[12,15] Therefore, we performed this study to examine the feasibility and safety of hemostatic spray powder for the prevention of delayed EP bleeding.

Recently, hemostatic spray powder was recommended as a second hemostatic modality for UGIB because it is applied to the mucosa and is eliminated within 24 h.[25] Several prior studies

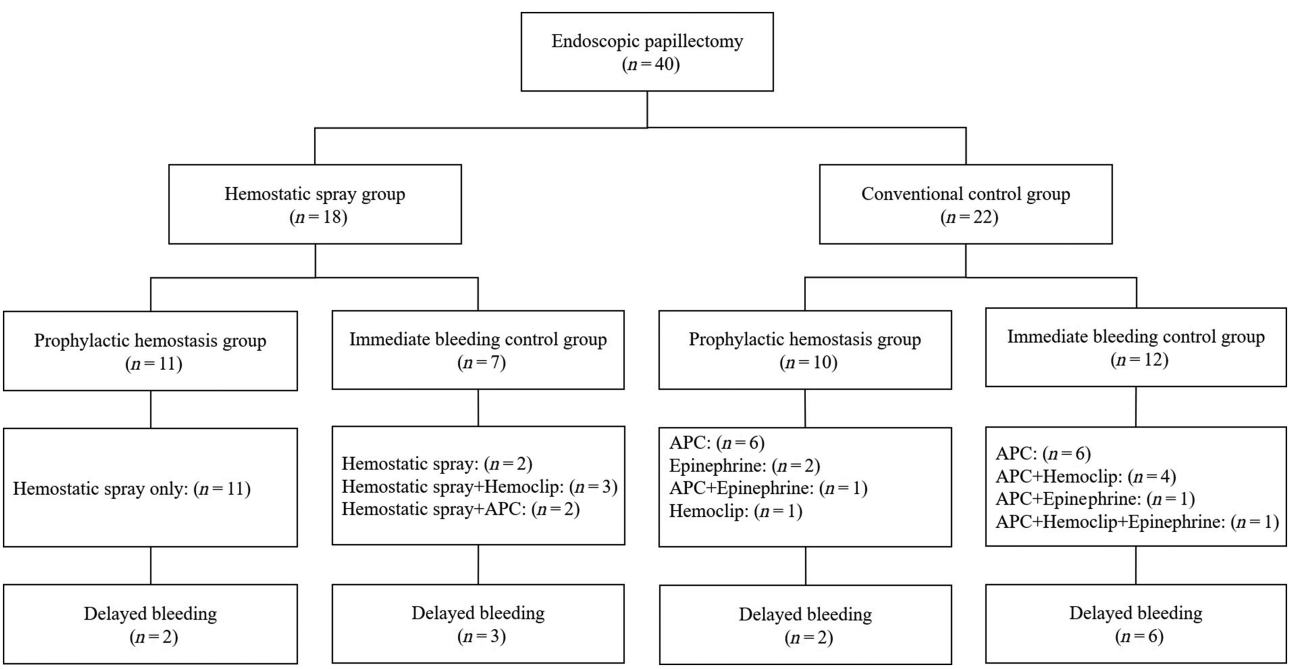

Figure 2 Flow chart of patient enrollment.

Table 2 Analysis of adverse events after endoscopic papillectomy according to the bleeding control methods

Variables, *n* (%)	Total (*n* = 40)	Hemostatic spray group (*n* = 18)	Conventional control group (*n* = 22)	*P*-value
Symptoms after EP				0.781
Melena or hematochezia	17 (42.5)	5 (27.8)	7 (31.8)	
Hematemesis	0	0	0	
Hemoglobin change (after 24 h)	0.6 ± 0.8	0.7 ± 0.9	0.4 ± 0.8	0.310
Delayed bleeding (after 24 h)	13 (32.5)	5 (27.8)	8 (36.4)	0.564
Asymptomatic hyperamylasemia	7 (17.5)	4 (22.2)	3 (13.6)	0.477
Post-ERCP pancreatitis	7 (17.5)	3 (16.7)	4 (18.2)	0.900
Mild	5	2	3	
Moderately severe	2	1	1	
Severe	0	0	0	
Cholangitis	0	0	0	
Perforation	0	0	0	

EP, endoscopic papillectomy; ERCP, endoscopic retrograde cholangiopancreatography.

have evaluated the efficacy of hemostatic spray on post-sphincterotomy bleeding. Sulz *et al*. reported 16 patients with UGIB of various origins.[26] Among these 16 patients, there were two patients with post-sphincterotomy bleeding. Hemostatic spray powder was applied with other conventional modalities, and hemostasis was achieved successfully without any complications.[26] Baracat *et al*. compared hemostatic spray and hemoclip in patients with UGIB.[27] In this study, a total of 39 patients were randomized into the hemostatic spray and hemoclip groups. The rebleeding rates did not differ between the two groups.[27] Four patients with post-sphincterotomy bleeding were included in the study, but subgroup analysis was not performed.

However, previous studies[11–15] on this topic were limited in that the sample sizes were too small to show that the hemostatic spray was effective for post-sphincterotomy bleeding, and no study has yet investigated the use of a hemostatic spray after EP. In the present study, we used Nexpowder, which consists of oxidized dextran and succinic acid modified amino acids, which are biodegradable and biocompatible.[28] When UI-EWD contacts water, the aldehyde group of the oxidized dextran reacts with the amine of the succinic acid modified amino acid, converting into an adhesive gel. The gel was physically transferred to the ulcer base to form a mechanical barrier to achieve hemostasis. Unlike thermal coagulation and hemostatic clips, a hemostatic spray has an advantage in that it is not necessary to target accurately. In our study, the hemostatic spray powder was applied for prophylactic or immediate hemostatic purposes. For prophylactic purposes, only a hemostatic spray powder was used in patients who did not suffer immediate post-EP bleeding. For immediate bleeding control, two patients received only hemostatic spray powder, whereas five patients received hemostatic spray following the use of conventional hemostatic modalities, which included hemoclip (*n* = 3) and APC (*n* = 2). The delayed bleeding rate after 24 h was 27.8% (5/18), regardless of the solo or combination treatment of hemostatic spray use. In the prophylactic hemostatic spray group, the delayed bleeding rate was 18.1%, which was similar to that in the conventional control group and other reported studies.[12,22] Yang *et al*. performed prophylactic APC to prevent delayed bleeding after EP, and the rebleeding rate was 30.8%.[12] For those patients with immediate bleeding after EP, the delayed bleeding rate was high in the hemostatic spray group (42.8%) and the conventional control group (50%). Although the delayed bleeding rate was high in both groups, rescue treatments such as fully covered metal stent, embolization, and surgery were not required in any patients included in

Table 3 Predictive factor of delayed bleeding after endoscopic papillectomy

	Univariable		Multivariable		
	OR	*P*-value	OR	95% CI	*P*-value
Sex (Male)	1.08	0.906	1.52	0.26–8.71	0.635
Age	1.01	0.781	1.04	0.95–1.13	0.398
Hypertension	0.47	0.302	0.09	0.01–2.19	0.140
Diabetes mellitus	3.55	0.139	9.64	0.65–141.78	0.098
Antiplatelet use	1.05	0.962	1.98	0.16–24.69	0.593
Epinephrine injection before EP	1.45	0.582	0.80	0.13–4.88	0.810
Resection method (en-bloc)	0.46	0.596	0.07	0.01–4.73	0.224
Tumor size	0.90	0.304	1.01	0.75–1.34	0.943
Final pathology[†]	0.51	0.459	0.35	0.02–6.22	0.482
Hemostatic spray group (*vs* conventional control group)	0.67	0.565	1.23	0.21–7.12	0.811

EP, endoscopic papillectomy.

[†]High-grade dysplasia adenoma + adenocarcinoma *versus* low-grade dysplasia adenoma + neuroendocrine tumor.

our study. However, further studies are needed to reduce delayed bleeding in patients with immediate bleeding control after EP.

There is a concern that, as the hemostatic spray powder scatters, pancreatic and bile duct blockage can lead to pancreatitis and cholangitis. In our study, the hemostatic spray powder was applied only when the pancreatic duct stent was inserted. The safety of applying hemostatic spray powder without the insertion of a pancreatic stent has not yet been established. Additionally, pancreatic duct stenting is usually recommended to prevent post-EP pancreatitis. In our study, 16.7% (3/18) and 22.2% (4/18) of patients developed post-EP pancreatitis and asymptomatic hyperamylasemia, respectively, but all recovered with conservative care. The overall incidence of pancreatitis observed in this study is similar to the conventional control group and consistent with the data reported in previous studies (3–45.3%).[3,5] Only one patient failed to biliary stent insertion in hemostatic spray group, but cholangitis did not develop. Beatrice *et al*. applied fibrin glue in patients with refractory immediate or delayed bleeding for post-sphincterotomy bleeding and post-EP bleeding.[22] Fibrin glue also has concerns of biliary and pancreatic drainage obstruction due to the intraductal fibrin clots. All patients underwent biliary drainage, and 42.8% (30/70) of patients underwent pancreatic drainage. The authors reported no cases of pancreatitis, despite the absence of pancreatic drainage. Further research is needed to determine whether pancreatitis occurs after hemostatic spray use in the absence of pancreatic drainage.

Our study had several limitations. First, as the first feasibility study of hemostatic spray after EP, it was only a clinical, retrospective feasibility study with a small sample size. Second, the purposes of hemostatic spray use differed between patients, and adjunctive conventional hemostatic methods were used together. Therefore, it is difficult to accurately determine the effectiveness of hemostatic spraying or other conventional modalities like hemoclipping in delayed bleeding. Third, we did not judge the cost-effectiveness of this approach. Notwithstanding these limitations, this study was the first study to evaluate the effectiveness of hemostatic spray after EP and compare with conventional modalities.

In conclusion, our study demonstrated that hemostatic spraying was technically feasible and safe for the prevention of delayed bleeding or immediate bleeding control after EP. Although either hemostatic spray or conventional bleeding control showed similar bleeding control rates, hemostatic spray group showed a decreased tendency of delayed bleeding. Therefore, hemostatic spraying may be a useful alternative to hemostatic modality in terms of convenience and efficacy. However, larger comparative and well-designed studies are warranted to confirm our results.

References

1 Fritzsche JA, Fockens P, Barthet M *et al*. Expert consensus on endoscopic papillectomy using a Delphi process. *Gastrointest. Endosc.* 2021; **94**: 760–73.
2 Vanbiervliet G, Strijker M, Arvanitakis M *et al*. Endoscopic management of ampullary tumors: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2021; **53**: 429–48.
3 De Palma GD. Endoscopic papillectomy: indications, techniques, and results. *World J. Gastroenterol.* 2014; **20**: 1537–43.
4 Han J, Kim MH. Endoscopic papillectomy for adenomas of the major duodenal papilla (with video). *Gastrointest. Endosc.* 2006; **63**: 292–301.
5 Ito K, Fujita N, Noda Y. Endoscopic diagnosis and treatment of ampullary neoplasm (with video). *Dig. Endosc.* 2011; **23**: 113–7.
6 Han J, Lee DW, Kim HG. Recent advances in endoscopic papillectomy for ampulla of vater tumors: endoscopic ultrasonography, intraductal ultrasonography, and pancreatic stent placement. *Clin. Endosc.* 2015; **48**: 24–30.
7 Fazel A, Quadri A, Catalano MF, Meyerson SM, Geenen JE. Does a pancreatic duct stent prevent post-ERCP pancreatitis? A prospective randomized study. *Gastrointest. Endosc.* 2003; **57**: 291–4.
8 Harewood GC, Pochron NL, Gostout CJ. Prospective, randomized, controlled trial of prophylactic pancreatic stent placement for endoscopic snare excision of the duodenal ampulla. *Gastrointest. Endosc.* 2005; **62**: 367–70.
9 Elmunzer BJ, Scheiman JM, Lehman GA *et al*. A randomized trial of rectal indomethacin to prevent post-ERCP pancreatitis. *N. Engl. J. Med.* 2012; **366**: 1414–22.
10 Akshintala VS, Sperna Weiland CJ, Bhullar FA *et al*. Non-steroidal anti-inflammatory drugs, intravenous fluids, pancreatic stents, or their combinations for the prevention of post-endoscopic retrograde cholangiopancreatography pancreatitis: a systematic review and network meta-analysis. *Lancet Gastroenterol. Hepatol.* 2021; **6**: 733–42.
11 Nam K, Song TJ, Kim RE *et al*. Usefulness of argon plasma coagulation ablation subsequent to endoscopic snare papillectomy for ampullary adenoma. *Dig. Endosc.* 2018; **30**: 485–92.
12 Yang JK, Hyun JJ, Lee TH *et al*. Can prophylactic argon plasma coagulation reduce delayed post-papillectomy bleeding? A prospective multicenter trial. *J. Gastroenterol. Hepatol.* 2021; **36**: 467–73.
13 Kagawa K, Kubota K, Kurita Y *et al*. Effect of preventive closure of the frenulum after endoscopic papillectomy: A prospective pilot study. *J. Gastroenterol. Hepatol.* 2020; **35**: 374–9.
14 Park SW, Song TJ, Park JS *et al*. Effect of prophylactic endoscopic clipping for prevention of delayed bleeding after endoscopic papillectomy for ampullary neoplasm: a multicenter randomized trial. *Endoscopy* 2022; **54**: 787–94.
15 Hyun JJ, Lee TH, Park JS *et al*. A prospective multicenter study of submucosal injection to improve endoscopic snare papillectomy for ampullary adenoma. *Gastrointest. Endosc.* 2017; **85**: 746–55.
16 Park JS, Kim HK, Shin YW, Kwon KS, Lee DH. Novel hemostatic adhesive powder for nonvariceal upper gastrointestinal bleeding. *Endosc. Int. Open* 2019; **7**: E1763–7.
17 Hussein M, Alzoubaidi D, Lopez MF *et al*. Hemostatic spray powder TC-325 in the primary endoscopic treatment of peptic ulcer-related bleeding: multicenter international registry. *Endoscopy* 2021; **53**: 36–43.
18 Shin J, Cha B, Park JS *et al*. Efficacy of a novel hemostatic adhesive powder in patients with upper gastrointestinal tumor bleeding. *BMC Gastroenterol.* 2021; **21**: 40.
19 Laine L, Barkun AN, Saltzman JR, Martel M, Leontiadis GI. ACG Clinical Guideline: Upper Gastrointestinal and Ulcer Bleeding. *Am. J. Gastroenterol.* 2021; **116**: 899–917.
20 Gralnek IM, Stanley AJ, Morris AJ *et al*. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy* 2021; **53**: 300–32.
21 ASGE Standards of Practice Committee, Anderson MA, Fisher L *et al*. Complications of ERCP. *Gastrointest. Endosc.* 2012; **75**: 467–73.

22 Orlandini B, Schepis T, Tringali A *et al*. Fibrin glue injection: Rescue treatment for refractory post-sphincterotomy and post-papillectomy bleedings. *Dig. Endosc.* 2021; **33**: 815–21.
23 Draganov PV, Wang AY, Othman MO, Fukami N. AGA Institute Clinical Practice Update: Endoscopic Submucosal Dissection in the United States. *Clin. Gastroenterol. Hepatol.* 2019; **17**: 16–25.e1.
24 Lin WC, Lin HH, Hung CY, Shih SC, Chu CH. Clinical endoscopic management and outcome of post-endoscopic sphincterotomy bleeding. *PLoS ONE* 2017; **12**: e0177449.
25 Chen YI, Barkun AN. Hemostatic powders in gastrointestinal bleeding: a systematic review. *Gastrointest. Endosc. Clin. N. Am.* 2015; **25**: 535–52.
26 Sulz MC, Frei R, Meyenberger C, Bauerfeind P, Semadeni GM, Gubler C. Routine use of hemospray for gastrointestinal bleeding: prospective two-center experience in Switzerland. *Endoscopy* 2014; **46**: 619–24.
27 Baracat FI, de Moura DTH, Brunaldi VO *et al*. Randomized controlled trial of hemostatic powder versus endoscopic clipping for non-variceal upper gastrointestinal bleeding. *Surg. Endosc.* 2020; **34**: 317–24.
28 Bang B, Lee E, Maeng J *et al*. Efficacy of a novel endoscopically deliverable muco-adhesive hemostatic powder in an acute gastric bleeding porcine model. *PLoS ONE* 2019; **14**: e0216829.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Video S1. A video of the prophylactic hemostatic spray use after endoscopic papillectomy. After endoscopic papillectomy, the hemostatic spray was applied to the resected lesion with spraying device under direct duodenoscopic vision.

Video S2. A video of the immediate minor bleeding control using hemostatic spray after endoscopic papillectomy. After endoscopic papillectomy, there was a bleeding with oozing pattern at the resected lesion. The hemostatic spray was applied to the resected lesion with spraying device under direct duodenoscopic vision.

Video S3. A video of the hemostatic spray use adjunctive to hemoclips after endoscopic papillectomy. After endoscopic papillectomy, two hemoclips were applied to the bleeding lesion and hemostatic spray was applied with spraying device under direct duodenoscopic vision.