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Clinical Changes in Emergency Endoscopic Hemostasis for Gastroduodenal Ulcer

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ABSTRACT

Introduction: This study aimed to examine the endoscopic hemostasis methods and characteristics of patients with gastroduodenal ulcer by comparing two sets of 5-year data. Included in this study are patients who were treated with emergency upper gastrointestinal endoscopy in our hospital over a 10-year study period.

Methods: Patients with hemorrhagic gastroduodenal ulcers who were treated with endoscopic hemostasis via emergency upper gastrointestinal endoscopy in our hospital from January 2004 to December 2008 and from January 2014 to December 2018 were categorized into Groups A and B, respectively. The two groups were retrospectively compared with regard to patient characteristics, hemostasis method, and various risk factors.

Results: Endoscopic hemostasis cases tended to decrease (202 vs. 130 cases, $p = 0.86$). The mean patient age increased (60.4 vs. 67.2 years, $p < 0.05$). There was no difference in the *Helicobacter pylori* infection rates (92.6% vs. 91.5%, $p = 0.89$). The number of patients taking oral proton-pump inhibitors (5.9% vs. 26.2%, $p < 0.05$), oral nonsteroidal anti-inflammatory drugs (17.3% vs. 31.5%, $p < 0.05$), and oral antithrombotic agents (15.3% vs. 28.5%, $p < 0.05$) was increased. The number of patients who underwent endoscopic clipping method (73.3% vs. 34.6%, $p < 0.05$) was reduced. The number of patients who underwent cauterization using hemostatic forceps significantly increased (4.0% vs. 76.2%, $p < 0.05$).

Conclusions: There was no difference in *H. pylori* infection rates due to the progressive aging of the patients. Fewer cases were treated using endoscopic clipping, whereas more cases were subjected to cauterization using hemostatic forceps.

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KEYWORDS: emergency endoscopy, hemorrhagic gastroduodenal ulcers, upper gastrointestinal endoscopy, cauterization, *Helicobacter pylori*

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Introduction

Upper gastrointestinal bleeding is a condition commonly encountered in routine clinical practice. It has an annual incidence of approximately 100 cases per 100,000 people. In particular, hemorrhagic gastroduodenal ulcers are still frequently encountered in emergency endoscopy.¹⁾ *Helicobacter pylori* infection is the main cause of gastroduodenal ulcers in addition to the use of corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and antithrombotic agents.²⁻⁴⁾

H. pylori infection causes gastric mucosal inflammation, is responsible for the atrophy of gastric mucosa and decreased gastric acid secretion, and leads to gastric and duodenal ulcers. Clinical studies have demonstrated that eradicating *H. pylori* improves gastric mucosal inflammation, thereby removing the factor that contributes to the development of ulcers and markedly inhibiting the recurrence of ulcers. Consequently, the use of proton-pump inhibitors (PPIs)⁵⁾ and spread of *H. pylori* eradication treatment^{6,7)} have been predicted to be accompanied by a decrease in upper gastrointestinal bleeding. Although *H. pylori* eradication therapy has been used widely, the aging society has led to a tendency toward an increase in morbidity of underlying diseases, cerebral and cardiovascular diseases, and orthopedic disorders.

Various comparative studies have previously been conducted to compare the techniques used in endoscopic hemostasis; however, thus far, it has been impossible to know which techniques are superior and which are inferior. In particular, for initial hemostasis and rebleeding, comparisons among the epinephrine local injection, pure ethanol local injection, hemostatic forceps, and endoscopic clipping methods have shown no difference in terms of the treatment effect.^{8,9)} Thus far, the endoscopic clipping method has been the primary technique employed for endoscopic hemostasis. However, because of recent advances in endoscopic treatments such as endoscopic submucosal dissection, hemostasis using high-frequency coagulation for preventing postoperative bleeding is often used as a simple and reliable treatment method.

With time, therefore, the characteristics of patients with hemorrhagic gastroduodenal ulcers and clinical features of hemostatic treatments are presumed to change. Thus, this retrospective study examined endoscopic hemostasis methods and characteristics of patients with gastroduodenal ulcer who were treated with emergency upper gastro-

intestinal endoscopy in our hospital by comparing two sets of 5-year data.

Methods

Patient groups

Patients who had undergone emergency upper gastrointestinal endoscopy in our hospital over the 5-year period from January 2004 to December 2008 and over the 5-year period from January 2014 to December 2018 were categorized into two groups based on the treatment period. In addition, we compared cases of gastric ulcer that required endoscopic treatment, defining 2004-2008 as Group A and 2014-2018 as Group B. In this study, emergency endoscopy was defined as endoscopy performed outside the predetermined consultation hours by the attending endoscopy specialist on duty within 12 h of visiting our hospital.

Classification of upper gastrointestinal ulcers

The characteristics of bleeding from peptic ulcers were classified as per the Forrest classification as follows: Ia, spurting bleeding; Ib, oozing bleeding; IIa, exposed blood vessels (nonbleeding visible vessels); IIb, adherent blood clot; IIc, presence of black spots as traces of bleeding on an ulcer base; and III, clean ulcer base.¹⁰⁾ Those with \geq stage IIa bleeding were treated with endoscopic hemostasis.

Patient characteristics

The two groups were retrospectively compared based on patient characteristics and endoscopic hemostasis methods. Among patient characteristics, the following risk factors of gastrointestinal bleeding were compared: age, sex, *H. pylori* infection, diabetes mellitus, and chronic renal failure in addition to the use of hemodialysis, PPIs, H₂-receptor antagonists (H₂-RAs), NSAIDs, antithrombotic drugs, and corticosteroids.

Endoscopic treatment methods

In our hospital, at least two endoscopy specialists are available on stand-by. When deemed necessary by the blood test results, computed tomography imaging findings, and the patient's general condition, an emergency endoscopy is performed within 12 h of the hospital visit. The endoscopic hemostasis technique was selected at the discretion of the attending endoscopy specialist and comprised either a mechanical method, namely the endoscopic clipping, or methods that use local injections, namely a local injection of pure ethanol and local injection of hypertonic sodium epinephrine (HSE), argon plasma coagulation, or coagulation hemostasis using hemostatic forceps with soft coagulation mode 50-60 W (Coregrasper; Olympus Co.,

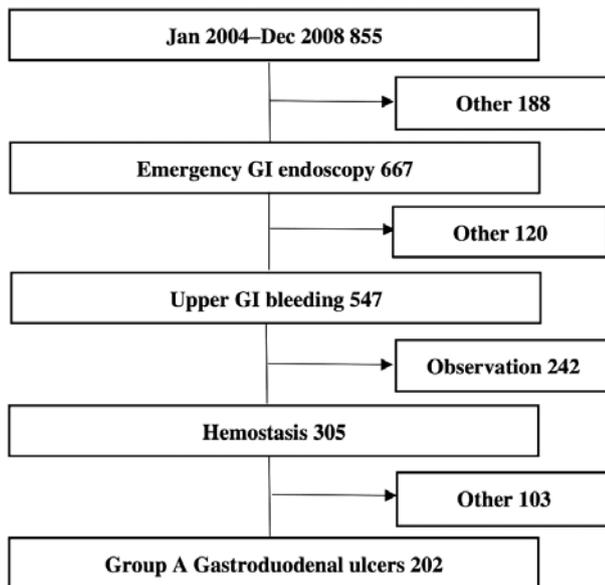


Fig. 1 Chart showing the cases of emergency endoscopy from 2004 to 2008 (Group A).

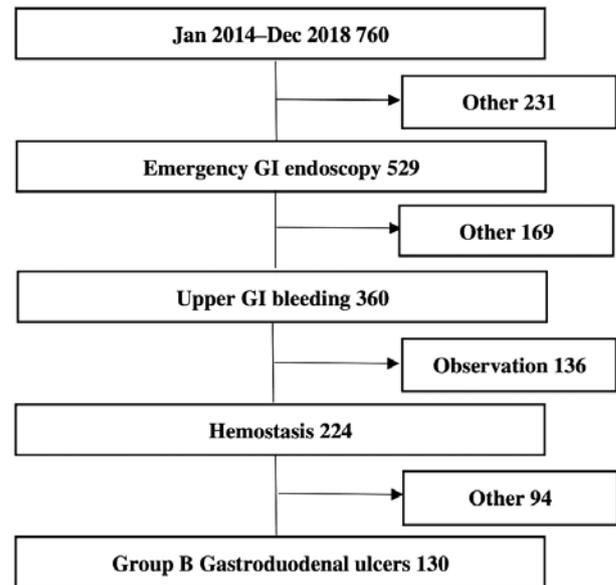


Fig. 2 Chart showing the cases of emergency endoscopy from 2014 to 2018 (Group B).

Japan). Rebleeding was defined as bleeding during hospitalization that required another round of hemostasis. All patients were administered an intravenous drip infusion of a PPI or an H₂-RA immediately before or after endoscopic treatment. In cases where patients had been taking oral corticosteroids, NSAIDs, or antithrombotic agents, all medications were discontinued if possible.

Statistical analyses and ethical approval

For statistical analysis, the Mann-Whitney U-test, chi-squared test, and Fisher's exact test were performed. Fisher's exact test was used when at least one expected frequency was <5. All analyses were performed using the software package EZR 1.41 (Saitama Medical Center, Jichi Medical University, Japan). A p-value of <0.05 was considered statistically significant. This study was conducted with the approval of the Ethics Committee of Toho University Omori Medical Center (approval number M20220). Requirement of written informed consent was waived owing to retrospective anonymized data collection.

Results

Emergency endoscopy cases

The overall number of emergency endoscopy cases was 855 in 2004-2008 and 760 in 2014-2018, respectively. The cases of both upper endoscopy (667 vs. 529) and upper gastrointestinal bleeding (547 vs. 360) were decreased in Group B during the two periods (Figs. 1, 2). Gastric ulcers were the most common type in both groups, followed by

esophagogastric varices and gastric duodenal ulcers (Figs. 3, 4). The proportion of patients with upper gastrointestinal bleeding requiring hemostatic treatment increased from 55.8% (305/547) in 2004-2008 to 62.2% (224/360) in 2014-2018. Therefore, a tendency for the rate of upper gastrointestinal bleeding to increase was observed. A total of 36.9% of patients with gastroduodenal ulcer and upper gastrointestinal bleeding required hemostatic treatment from 2004 to 2008 (Group A: 202/547) compared with 36.1% from 2014 to 2018 (Group B: 130/360). Thus, no change was observed between the groups ($p = 0.86$).

Patient characteristics

The comparison between Groups A and B in terms of patients with gastroduodenal ulcers who underwent hemostatic treatment showed that Group B patients were older (age: 60.4 vs. 67.2 years, $p < 0.05$; Table 1). In terms of sex, the proportion of women increased from Group A to Group B (22.3% vs. 33.9%, respectively; $p < 0.05$). A comparison of the two groups in terms of the bleeding sites showed that gastric ulcers overall accounted for 78.2% of the bleeding sites in Group A and 76.2% in Group B; these values did not differ significantly. Duodenal ulcers accounted for 21.8% and 23.8% ($p = 0.64$) of the bleeding sites in Groups A and B, respectively, which also did not differ significantly. There was no difference between the two groups with respect to the lesion sites located in the upper, middle, or lower portion of the stomach ($p = 0.83$). Likewise, the two groups did not differ in their Forrest

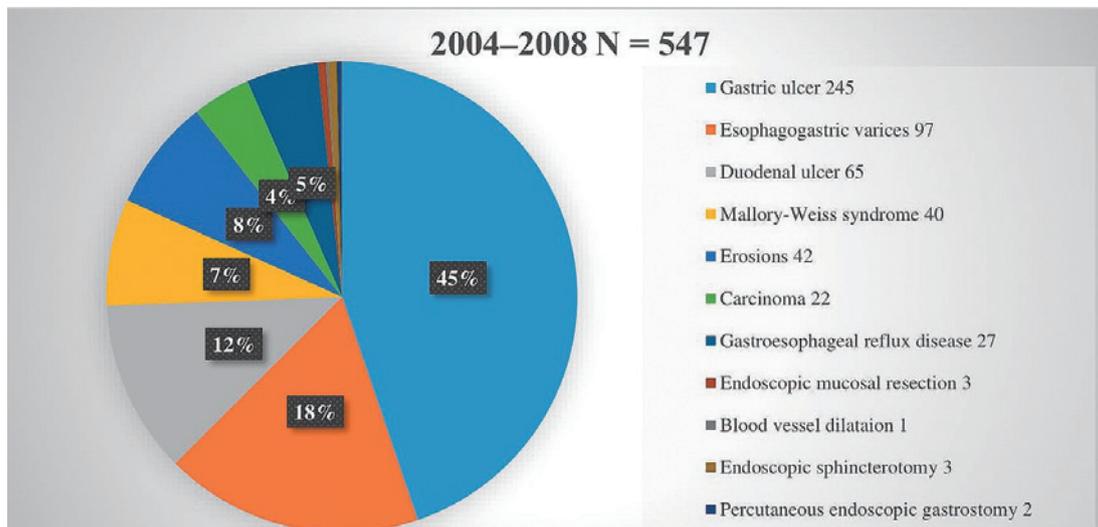


Fig. 3 Pie chart showing the frequencies of diseases that caused upper gastrointestinal bleeding from 2004 to 2008 (N = 547) (Group A).

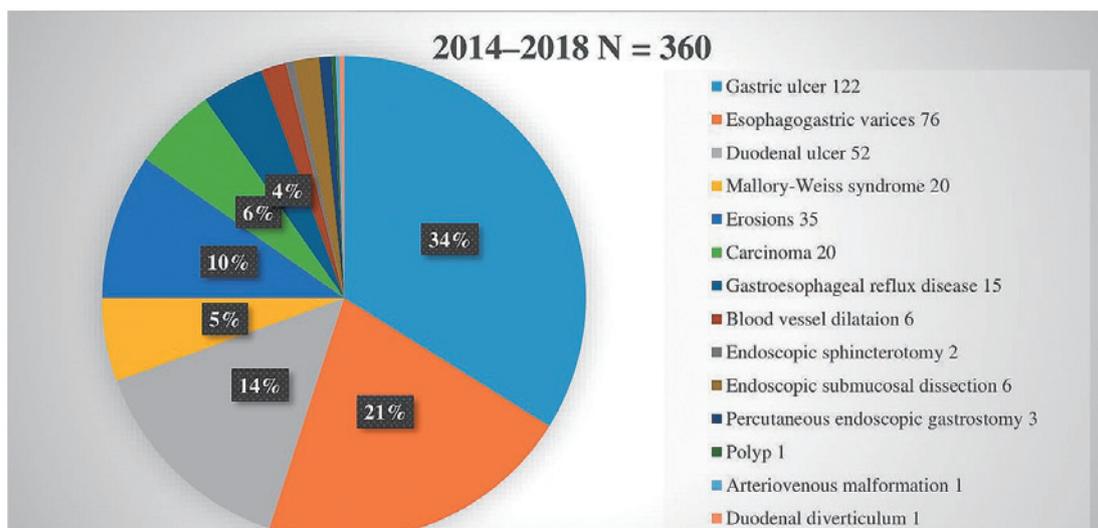


Fig. 4 Pie chart showing the frequencies of diseases that caused upper gastrointestinal bleeding from 2014 to 2018 (N = 360) (Group B).

classification ($p = 0.26$; Table 2). A comparison of patient characteristics in terms of risk factors showed that the *H. pylori* infection rate did not differ between the two groups (92.6% vs. 91.5%, $p = 0.89$). Moreover, no change was found in terms of comorbidities, namely, diabetes mellitus (12.9% vs. 20.8%, $p = 0.08$) and chronic renal failure (9.9% vs. 13.1%, $p = 0.47$), or in terms of the proportion of patients on dialysis (5.5% vs. 8.5%, $p = 0.39$; Table 1).

More patients took oral PPIs (5.9% vs. 26.2%, $p < 0.05$), oral NSAIDs (17.3% vs. 31.5%, $p < 0.05$), and oral antithrombotic agents (15.3% vs. 28.5, $p < 0.05$) in Group A

than in Group B. The groups did not differ in their oral intake of H₂-RA (9.9% vs. 4.6%, $p = 0.12$) and corticosteroids (5.5% vs. 7.7%, $p = 0.56$; Table 1).

Selection of the endoscopic hemostasis technique

Regarding the endoscopic hemostasis technique used, endoscopic clipping (73.3% vs. 34.6%, $p < 0.05$), local injections of pure ethanol (34.2% vs. 1.5%, $p < 0.05$), and local injections of HSE (49.0% vs. 32.3%, $p < 0.05$) showed significant decreases in Group B than in Group A. Cauterization using hemostatic forceps showed a significant increase (4.0% vs. 76.2%, $p < 0.05$) in Group B than in Group A.

Table 1 Patient characteristics (including orally administered medications) / background

Characteristics	Group A (N = 202)	Group B (N = 130)	P
Age (range)	60.4 (13–89)	67.2 (14–88)	<0.05 *
Male	157 (77.7%)	86 (66.2%)	<0.05
Female	45 (22.3%)	44 (33.9%)	
<i>H. pylori</i>	187 (92.6%)	119 (91.5%)	0.89
Diabetes	26 (12.9%)	27 (20.8%)	0.08
Chronic renal failure	20 (9.9%)	17 (13.1%)	0.47
Hemodialysis	11 (5.5%)	11 (8.5%)	0.39
PPIs	12 (5.9%)	34 (26.2%)	<0.05
NSAIDs	35 (17.3%)	41 (31.5%)	<0.05
Antithrombotic drug	31 (15.3%)	37 (28.5%)	<0.05
Corticosteroid	11 (5.5%)	10 (7.7%)	0.56

PPIs, proton pump inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs
Chi-squared test; *: Mann–Whitney *U*-test

Table 2 Bleeding sites and Forrest classification

Location	Group A (N = 202)	Group B (N = 130)	P
Stomach	158 (78.2%)	99 (76.2%)	0.64
Upper	44 (27.9%)	26 (26.3%)	0.83
Middle	44 (27.9%)	26 (26.3%)	
Lower	70 (44.3%)	47 (47.5%)	
Duodenum	44 (21.8%)	31 (23.8%)	0.64
Forrest classification			
Ia	11 (5.4%)	3 (2.3%)	0.26 **
Ib	93 (46.0%)	55 (42.0%)	
IIa	98 (48.5%)	72 (55.4%)	

Chi-squared test; **: Fisher's exact test

Table 3 Hemostasis method (gastric and duodenal ulcers), duration of procedure, and rebleeding

Hemostasis method	Group A (N = 202)	Group B (N = 130)	P
Clipping	148 (73.3%)	45 (34.6%)	<0.05
HSE *	99 (49.0%)	42 (32.3%)	<0.05
Pure ethanol	69 (34.2%)	2 (1.5%)	<0.05 **
Cauterization	8 (4.0%)	99 (76.2%)	<0.05
Average time (range in min)	39.5 (12–109)	27.0 (9–98)	<0.05 *
Standard deviation (SD)	17.4	15.2	
Rebleeding	22 (10.9%)	8 (6.2%)	0.20

HSE, hypertonic sodium epinephrine

Chi-squared test; *: Mann–Whitney *U*-test; **: Fisher's exact test

Partly due to the widespread use of hemostasis via cauterization, the duration of the endoscopic hemostasis procedure was significantly shorter (39.5 vs. 27.0 min, $p < 0.05$) and frequency of rebleeding tended to decrease (22/202 [10.9%] vs. 8/130 [6.2%], $p = 0.20$) in Group B (Table 3).

Hemostasis method for duodenal ulcer

For the duodenum only, the endoscopic clipping method (72.7% vs. 74.2%, $p = 0.61$) showed no difference, whereas cauterization using hemostatic forceps increased significantly (2.3% vs. 41.9%, $p < 0.05$) in Group B than in Group

Table 4 Hemostasis method (duodenal ulcer)

Hemostasis method	Group A (N = 44)	Group B (N = 31)	P
Clipping	32 (72.7%)	23 (74.2%)	0.61
HSE *	18 (40.9%)	6 (19.4%)	0.09
Pure ethanol	8 (18.2%)	0 (0.0%)	<0.05 **
Cauterization	1 (2.3%)	13 (41.9%)	<0.05 **

HSE, hypertonic sodium epinephrine

Chi-squared test; **: Fisher's exact test

A (Table 4).

Discussion

Compared with Group A, the number of upper gastrointestinal bleeding cases tended to decrease, patients tended to be older, and the proportion of women increased in Group B. This may be due to the high infection rate of *H. pylori* in the elderly people¹¹⁾ and the increase in the proportion of women in the Japanese population as a result of the increased life expectancy of Japanese women.^{12, 13)}

The *H. pylori* infection rates have been decreasing in several countries, including Japan.¹⁴⁾ However, in this study, the two groups did not differ significantly in their infection rates. We attribute this result to the following two reasons. First, this study was limited to patients with gastroduodenal ulcer who had undergone endoscopic hemostasis. Second, as Group B comprised older patients, it also had more patients infected with *H. pylori*.

Chronic diseases such as diabetes and renal failure are known risk factors of upper gastrointestinal bleeding. Patients with diabetes frequently suffer from gastroduodenal ulcers due to microcirculatory disorders that affect atrophic change of mucosa, neuropathy, and mucus secretion disorders.¹⁵⁾ Patients with chronic renal failure undergoing dialysis treatment have a tenfold higher risk of developing upper gastrointestinal bleeding as a complication.¹⁶⁾ However, in this study, these factors did not differ among the two groups, indicating that chronic diseases are not affected by upper gastrointestinal bleeding.

The evaluation of the oral medications revealed that more Group B patients were taking oral PPIs, NSAIDs, and antithrombotic agents. The increase in the number of patients taking oral PPIs may have contributed to the decrease in the total number of patients with gastroduodenal ulcers. However, this study failed to demonstrate whether there was a decrease in the risk of developing ulcers that required hemostatic treatment. The increase in the number of patients taking oral NSAIDs and antithrombotic

agents suggests that the need to prescribe these medications has increased, owing to the aging population. The risk of developing ulcers is 5.5 times higher in elderly individuals using NSAIDs, which is higher than that found in young individuals using NSAIDs (1.5 times).¹⁷⁻¹⁹⁾ Reports on antithrombotic agents have also indicated that the risk of gastrointestinal bleeding is approximately 5.5 times higher in older than in younger adults.²⁰⁻²³⁾ Moreover, studies have shown that patients taking oral antithrombotic agents and NSAIDs account for approximately 50% of patients with gastrointestinal bleeding.^{24, 25)} Thus, patients taking oral NSAIDs and antithrombotic agents must be carefully observed owing to the possibility of peptic ulcer development.

Endoscopic hemostasis is the first-line therapy for gastrointestinal bleeding,²⁶⁾ and the success rate of hemostasis in treating upper gastrointestinal bleeding is $\geq 90\%$. In the present study, the number of patients treated using the endoscopic clipping method as a technique for endoscopic hemostasis decreased markedly, whereas the number of cauterization cases using hemostatic forceps increased noticeably.

The endoscopic clipping method requires the device to be replaced each time. In patients taking antithrombotic drugs, it is easier to bleed from the clip site, making visualization from the front difficult, and it is not suitable for patients with severe fibrosed ulcer. It is a device that requires the skill of an endoscopy specialist. Cauterization using hemostatic forceps has been developed for hemostasis during endoscopic submucosal dissection (ESD). Cauterization has been increasingly used for gastroduodenal ulcer in recent years owing to its simplicity and reliability. In our hospital, starting from 2007, the number of ESD cases increased significantly, and cauterization using hemostatic forceps became the mainstream method. Furthermore, the present study found that the time required for hemostasis was significantly shorter, and the proportion of cases of rebleeding tended to be lower. The tech-

nique is believed to allow less experienced endoscopy specialists to achieve a highly reliable hemostatic effect.²⁷⁾ The frequency of pure ethanol injections decreased, but that of local HSE solution injections remained unchanged in the present study. Pure ethanol injections are no longer used as they lead to the enlargement of the ulcer after the procedure. The advantages of HSE solution are that it has only a weak tissue-damaging effect, can be frequently administered via local injections, and can be used in the duodenum.

The endoscopic clipping method was the most frequently performed hemostasis technique for duodenal ulcers (72.7% vs. 74.2%, $p = 0.61$), followed by cauterization with hemostatic forceps (2.3% vs. 41.9%, $p < 0.05$), and the risk of perforation was considered during cauterization with hemostatic forceps. Cauterization of the duodenum with bipolar hemostats rather than monopolar hemostats is safer because it reduces the risk of delayed perforation.²⁸⁾ Hemostatic forceps will be widely used for the hemostasis of duodenal ulcers owing to the development and spread of high-frequency hemostatic forceps devices.

This study is associated with some limitations. First, this study had a small sample size. Second, because this study relies on the retrospective analysis of data from a single institution, the data from other institutions have not been verified. In the future, more institutions must be included to increase the number of endoscopic hemostasis procedures being analyzed.

In conclusion, there was no difference in the rate of *H. pylori* infection in the gastroduodenal ulcers that required hemostatic treatment. Hemostasis methods have undergone significant changes owing to the widespread use of cauterization with hemostatic forceps. Moreover, with the development and widespread use of high-frequency hemostatic devices, we expect that hemostatic forceps will be widely used in the hemostasis of duodenal ulcers.

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Authors' contribution: Dan and Igarashi designed the study. Dan, Hijikata, Fuchinoue, Toba, and Kikuchi collected the data. Yamaguchi and Dan analyzed the data. Dan wrote the manuscript.

Ethics statement: This study was performed with the approval of the Ethics Committee of the Toho University Medical Center Omori Hospital (M20220).

Conflicts of interest: None declared.

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