

Evaluation of hemostasis with soft coagulation using endoscopic hemostatic forceps in comparison with metallic hemoclips for bleeding gastric ulcers: a prospective, randomized trial

Seiichiro Arima · Yasuhisa Sakata · Shinichi Ogata · Naoyuki Tominaga · Nanae Tsuruoka · Kotaro Mannen · Ryosuke Shiraishi · Ryo Shimoda · Seiji Tsunada · Hiroyuki Sakata · Ryuichi Iwakiri · Kazuma Fujimoto

Received: 8 November 2009 / Accepted: 3 December 2009 / Published online: 25 December 2009
© Springer 2009

Abstract

Background Endoscopic high-frequency soft coagulation, recently developed in Japan, is available for the management of gastric bleeding in cases of bleeding gastric ulcers and bleeding during endoscopic submucosal dissection. The aim of this study was to evaluate the efficacy of hemostasis with soft coagulation for bleeding gastric ulcers by comparing it with hemoclips in a prospective, randomized trial.

Methods During the period of April 2006 to March 2008, 96 patients that had gastric ulcers with bleeding or nonbleeding visible vessels were enrolled in this study. All of the 96 patients were randomly divided into two groups: endoscopic hemostasis with soft coagulation (Group I) or endoscopic hemoclippping (Group II).

Results A total of 41 (85%) out of 48 patients in Group I and 38 (79%) out of 48 patients in Group II were successfully treated with soft coagulation or clipping alone, respectively. The endoscopic hemostasis rate for the initial modality in combination with another endoscopic procedure performed after the initial method was 98% in both groups. One patient in Group I (2%) and five patients in Group II (10%) experienced recurrent bleeding. The time required to achieve hemostasis was shorter in Group I

compared with Group II (9.2 ± 11.1 vs. 13.6 ± 9.4 min; $P < 0.05$).

Conclusions This study revealed that soft coagulation is as effective as hemoclippping for treating bleeding gastric ulcers. The time required to achieve hemostasis was shorter with the soft coagulation procedure.

Keywords Recurrent bleeding · Clip · Proton pump inhibitor · Visible vessels

Introduction

Since 1983, when Marshall and Warren [1] succeeded in isolating *Helicobacter pylori* (*H. pylori*) for the first time, the subsequent rapid accumulation of basic and clinical research has resulted in a marked change in the concept and treatment of upper gastrointestinal diseases. There is a close relationship between *H. pylori* infection and peptic ulcers [2], and much progress has been made in approaches to eradicate *H. pylori* in order to treat and/or prevent gastric and duodenal ulcers [3]. The eradication of *H. pylori* is known to reduce the recurrence of peptic ulcers [4, 5] and rehemorrhage [6]. However, upper gastrointestinal bleeding is still one of the most common and serious clinical complications of peptic ulcers [7–13]. In the past 25 years, various endoscopic hemostatic methods for bleeding ulcers have been developed, and endoscopic hemostasis is the first-choice treatment for upper gastrointestinal bleeding. These methods may be classified into three categories: thermal or electrical coagulation methods (e.g., heater probe, laser, electrocoagulation, and argon plasma coagulator), mechanical hemostatic methods (e.g., hemoclippping and banding), and local injection methods (e.g., pure ethanol, epinephrine, ethanolamine oleate, histoacryl, polidocanol).

S. Arima · Y. Sakata · N. Tominaga · N. Tsuruoka · K. Mannen · R. Shiraishi · R. Shimoda · S. Tsunada · H. Sakata · R. Iwakiri · K. Fujimoto (✉)
Department of Internal Medicine and Gastrointestinal Endoscopy, Saga Medical School, 5-1-1 Nabeshima, Saga 849-8501, Japan
e-mail: fujimoto@post.saga-med.ac.jp

S. Ogata
Saga Prefectural Hospital Koseikan, Saga, Japan

Soft coagulation with an electrosurgical unit using endoscopic hemostatic forceps, a type of high-frequency coagulation, is available for the management of gastric bleeding during endoscopic submucosal dissection [14]. This method might be applicable for the hemostasis of a bleeding gastric ulcer. To our knowledge, no prospective studies have evaluated its effects on bleeding ulcers. Therefore, the aim of this study was to evaluate the efficacy of soft coagulation for treating bleeding gastric ulcers by comparing it with hemoclips, which are commonly used for the hemostasis of bleeding gastric ulcers.

Materials and methods

Patients

Between April 2006 and March 2008, 96 patients with gastric ulcers with bleeding or non-bleeding visible vessels were enrolled in this study. A visible vessel was defined as a raised red or black spot that was resistant to gentle washing of the ulcer base [15, 16]. Before endoscopic examination, informed consent was obtained from all patients who received emergency endoscopy because of suspected gastro-intestinal bleeding. All of the consecutive 96 patients were randomized into one of two groups according to a table of random permutations, and the applied hemostasis method was determined before endoscopic examination. Group I was initially treated with soft coagulation. Group II was initially treated with clipping. When the endoscopist judged that the initial hemostasis was not completely obtained by the allocated method, any additional hemostatic method was performed. We compared the two groups in terms of initial hemostasis success with the allocated single method as well as treatment time required to achieve hemostasis (from the start of the application of clipping or soft coagulation to the attainment of initial hemostasis). Additionally, recurrent bleeding was evaluated. This study was performed according to the guidelines of the committee on clinical practice of Saga Medical School Hospital, and was approved by the institutional review boards.

Methods

Emergency endoscopy was performed as soon as possible, and within 3 h after visiting our hospital, by endoscopists with over 6 years of experience. No other medication, except lidocaine pharyngeal spray, was used for premedication. A forward-viewing endoscope (Q240, Q260, H260 or Q260J, Olympus, Tokyo, Japan) was used to examine the patients.

For the subjects in Group I, soft coagulation was performed using an electrosurgical unit (ICC200, ERBE

Elektronedizin, Tübingen, Germany) and monopolar hemostatic forceps (Radial Jaw™ 3 Hot Biopsy Forceps, Boston Scientific Co, Boston, MA, USA) inserted through the biopsy channel of the endoscope. When the covering clot adhered to the ulcer base, the endoscopist removed the clot using an irrigation system or the hemostatic forceps to detect the vessel. The closed forceps were gently pressed to the target and the endoscopist applied an electric current for 1–2 s. The output of the equipment was set from 50 to 80 W, and the endoscopist coagulated four sites surrounding the blood vessel initially and coagulated the blood vessel itself [17]. This soft coagulation process was repeated until hemostasis was confirmed.

For patients in Group II, hemoclips (HX-610-135, HX-610-135S, hemoclip, Olympus Optical, Tokyo, Japan) were placed on the ulcer base to bind the visible bleeding or nonbleeding vessels. When a vessel could not be visualized because of a massive clot covering the ulcer base, the clot was removed with an irrigation system. Hemoclippping was performed continuously until hemostasis was confirmed.

After the initial endoscopic hemostasis, all of the patients were given an intravenous H₂-receptor antagonist for 1–2 days during fasting. After confirming hemostasis by follow-up endoscopy, the patients were re-fed and given an oral proton pump inhibitor. In patients with unstable vital signs or continued tarry or bloody stools during the hospital stay, emergency endoscopy was performed to determine whether any additional treatment was needed. Rebleeding was defined as follows: (1) blood in the stomach 24 h after the initial treatment, or stigmata of a recent hemorrhage at the ulcer base, or (2) fresh hematemesis and/or melena accompanied by either shock or a fall in hemoglobin level of greater than 2.0 g/dl within a 24-h period. Patients who experienced rebleeding were treated with an endoscopic hemostatic treatment selected by the endoscopist, and which was deemed to be most appropriate for the individual patient. Transcatheter arterial embolization or emergency surgery was performed in the event of: (1) rebleeding that could not be treated with endoscopic therapy; (2) recurrent bleeding after the third endoscopic treatment, or; (3) the total amount of blood transfused being more than 2000 ml.

Evaluation of data

Initial hemostasis with the allocated method, recurrent bleeding, time to achieve hemostasis with the allocated method, and 30-day mortality (from the time of initial hemostasis) were evaluated and compared between the two groups. Recurrent bleeding was defined as rebleeding within 7 days after the initial hemostasis. Statistical analyses were carried out using χ^2 tests and Mann–Whitney's *U* test, as appropriate. Differences were considered significant if the probability of the difference occurring by chance was

less than 5 in 100 ($P < 0.05$). All results are expressed as mean \pm standard deviation (SD), unless otherwise stated.

Results

Table 1 shows the background characteristics of the patients in both groups. There were no significant differences between the two groups regarding age, sex ratio, ulcer history, hemoglobin level at emergency endoscopy, co-morbidities, anticoagulants and/or anti-platelet drug use, nonsteroidal anti-inflammatory drug use, and *H. pylori* infection. As shown in Table 2, the location of the gastric ulcer was not statistically different between the two groups. The bleeding state, as indicated by Forrest classification, and the sizes of the gastric ulcer and the visible vessel did not differ between the two groups. The years of experience of the endoscopists who performed the emergency endoscopy were not different in the two tested groups.

Table 3 shows the results of endoscopic hemostasis in both groups. Initial hemostasis with soft coagulation alone was successful in 41 (85%) out of the 48 patients in Group I. Initial hemostasis with clipping alone was successful in 38 (79%) out of 48 patients in Group II. The initial hemostasis rate with a single modality was not different between the two groups. The endoscopic hemostasis rate for the initial modality in combination with another endoscopic procedure performed after the initial method was 98% in both groups. Two patients (one patient in each group) were treated by transcatheter arterial embolization, and no patient required a surgical operation. One patient in Group I (2%) and five patients in Group II (10%) experienced recurrent bleeding within 7 days. The rebleeding rate

Table 1 Patient characteristics in the two tested groups

	Group I (n = 48)	Group II (n = 48)
Age	69.1 \pm 10.9	68.4 \pm 10.7
Sex ratio (males:females)	31:17	31:17
Ulcer history (+:–)	36:12	36:12
Hb (mg/dl)	8.8 \pm 2.6	8.3 \pm 2.8
Co-morbidities		
Hypertension	24	17
Diabetes mellitus	12	4
Anticoagulants and/or anti-platelet drug use	18	11
NSAID use	18	18
<i>H. pylori</i> infection	32	41

Values are mean \pm SD

Group I, patients treated with soft coagulation; Group II, patients treated with hemoclips; NSAIDs, nonsteroidal anti-inflammatory drugs

Table 2 Characteristics of the bleeding gastric ulcers

	Group I (n = 48)	Group II (n = 48)
Main location		
Upper part of the stomach	8	13
Middle part of the stomach	33	32
Lower part of the stomach	7	3
Forrest classification		
Ia	8	6
Ib	7	6
IIa	33	36
Size		
Ulcer size (mm)	17	22
Visible vessel size (mm)	1.4	1.5

Values are mean \pm SD

Group I, patients treated with soft coagulation; Group II, patients treated with hemoclips

Table 3 Hemostasis ratio, recurrent bleeding within 7 days, and time required to achieve hemostasis

	Group I (n = 48)	Group II (n = 48)
Initial hemostasis with single modality	41/48 (85%)	38/48 (79%)
Initial hemostasis combined with other endoscopic methods	47/48 (98%)	47/48 (98%)
Recurrent bleeding	1/48 (2%)	5/48 (10%)
Emergency surgery	0/48 (0%)	0/48 (0%)
Mortality within 1 month	1/48 (2%)	0/48 (0%)
Perforation	0/48 (0%)	0/48 (0%)
Required time for hemostasis (min)	9.2 \pm 11.1*	13.6 \pm 9.4

Values are mean \pm SD

Group I, patients treated with soft coagulation; Group II, patients treated with hemoclips

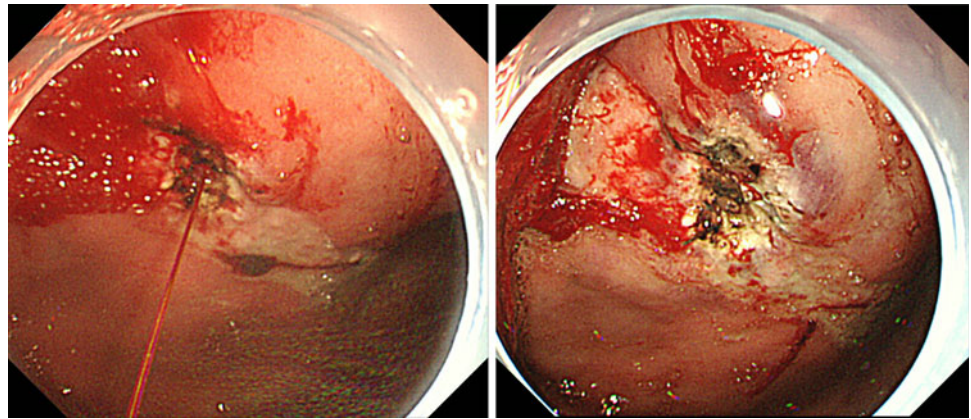
* $P < 0.05$ compared with Group II

tended to be higher in Group II, but the difference was not statistically significant. All of the patients with rebleeding were successfully treated by the endoscopic hemostasis method selected by the endoscopist. The time required to achieve hemostasis was significantly shorter in Group I compared with Group II (9.2 \pm 11.1 vs. 13.6 \pm 9.4 min; $P < 0.05$). One patient in Group I died within 1 month after the initial hemostasis because of lung cancer.

Discussion

Over the past 25 years, improvements in endoscopic hemostatic methods have provided safe and effective hemostasis. Several prospective controlled studies and

Fig. 1 Hemostasis of the bleeding gastric ulcer with soft coagulation



meta-analyses have demonstrated the efficacy of endoscopic hemostasis [18–32]. In these studies, endoscopic hemostasis was performed with local injection therapy, thermal coagulation therapy or mechanical hemostatic methods such as clipping, and there were few statistical differences between these procedures with regard to the hemostatic rate (ranging from 70.0 to 98.5%). Nevertheless, each procedure has advantages and drawbacks associated with the difficulty of the procedure, extent of tissue injury, and frequency of complications. The hemoclipping method for hemostasis was reported for endoscopic hemostasis, and several prospective randomized studies and a meta-analysis have demonstrated the efficacy of this method. In most of these studies, the permanent haemostatic rate with hemoclipping ranged from 89.0 to 98.5% [18–20, 31–34].

Hemostasis with soft coagulation performed using endoscopic hemostatic forceps was mainly introduced to manage bleeding during endoscopic submucosal dissection [14]. This coagulation method has now been widely utilized to manage cases of bleeding gastric ulcers in Japan. However, no prospective and/or randomized studies have evaluated the efficacy of soft coagulation for bleeding gastric ulcers. The present prospective randomized study evaluated whether the soft coagulation method was as effective as endoscopic hemoclipping for treating bleeding gastric ulcers. The results of this study indicate that the hemostasis rate with soft coagulation is equivalent to that with hemoclipping. Furthermore, the rate of rebleeding within 7 days tended to be lower with soft coagulation than with hemoclipping, and the time required to achieve hemostasis was shorter with soft coagulation than with hemoclipping. These findings can be considered advantages of the endoscopic soft coagulation method for treating bleeding gastric ulcers.

The soft coagulation method has some merits compared with the conventional thermal coagulation therapy. During soft coagulation, the tissue is coagulated without any carbonization or spark because the voltage is controlled below

200 V. The coagulated tissue is not peeled during coagulation, unlike in the conventional coagulation method, which might explain the low rate of recurrent bleeding in this study. In fact, as shown in Fig. 1, the coagulated tissue with high electrical resistance was not burned more than necessary. Another advantage of soft coagulation is the shallow depth of the coagulation tissue, which might prevent perforation after the therapeutic procedure. In fact, we did not experience any complications involving perforation in this study in either group.

There are several limitations associated with endoscopic soft coagulation. When the gastric ulcer is submerged in water and/or has a high volume of tissue, coagulation of the vessel may be difficult because of leaking electricity. Furthermore, devices for soft coagulation, including disposable hemostatic forceps, are relatively expensive compared with other hemostasis methods for treating bleeding gastric ulcers.

In conclusion, this study demonstrated that the novel endoscopic hemostatic method of soft coagulation was as effective as hemoclipping for treating bleeding gastric ulcers. In addition, the time required to achieve hemostasis with soft coagulation was shorter than that needed when using hemoclipping. Our findings suggest that soft coagulation should be considered for the hemostasis of bleeding gastric ulcers.

References

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomachs of patients with gastritis and peptic ulceration. *Lancet*. 1984;1:1311–4.
2. Schubert TT, Bologna SD, Nensy Y, Schubert AB, Mascha EJ, Ma CK. Ulcer risk factors, interactions between *Helicobacter pylori* infection, non-steroidal use, and age. *Am J Med*. 1993;94:413–8.
3. Hentschel E, Brandstatter G, Dragosics B, Hirschl AM, Nemeč H, Schütze K, et al. Effect of ranitidine and amoxicillin plus metronidazole on the eradication of *Helicobacter pylori* and the recurrence of duodenal ulcer. *N Engl J Med*. 1993;328:308–12.

4. Labenz J, Borsch G. Evidence for the essential role of *Helicobacter pylori* in gastric ulcer disease. *Gut*. 1994;35:19–22.
5. Van der Hulst RW, Rauws EA, Koycu B, Keller JJ, Bruno MJ, Tijssen JG, et al. Prevention of ulcer recurrence after eradication of *Helicobacter pylori*: a prospective long-term follow-up study. *Gastroenterology*. 1997;113:1082–6.
6. Kikkawa A, Iwakiri R, Ootani H, Ootani A, Fujise T, Sakata Y, et al. Prevention of the rehaemorrhage of bleeding peptic ulcer: effects of *Helicobacter pylori* eradication and acid suppression. *Aliment Pharmacol Ther*. 2005;21:79–84.
7. British Society of Gastroenterology Endoscopy Committee. Non-variceal upper gastrointestinal hemorrhage: guidelines. *Gut*. 2002;51:41–6.
8. Koyama T, Fujimoto K, Iwakiri R, Sakata H, Sakata Y, Yamaoka K, et al. Prevention of recurrent bleeding from gastric ulcer with a nonbleeding visible vessel by endoscopic injection of absolute ethanol: a prospective, controlled trial. *Gastrointest Endosc*. 1995;42:128–31.
9. Ootani H, Iwakiri R, Shimoda R, Nakahara S, Amemori S, Fujise T, et al. Role of *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drug use in bleeding gastric ulcers in Japan. *J Gastroenterol*. 2006;41:41–6.
10. Raju GS, Kaltenbach T, Soetikno R. Endoscopic mechanical hemostasis of GI arterial bleeding. *Gastrointest Endosc*. 2007;66:774–85.
11. Chan FK. Proton-pump inhibitors in peptic ulcer disease. *Lancet*. 2008;372:1198–200.
12. Yamaguchi M, Iwakiri R, Yamaguchi K, Mizuta T, Shimoda R, et al. Bleeding and stenosis caused by reflux esophagitis was not common in emergency endoscopic examination: a retrospective patient chart review at a single institution in Japan. *J Gastroenterol*. 2008;43:265–9.
13. Shimoda R, Iwakiri R, Sakata H, Ogata S, Ootani H, Sakata Y, et al. Endoscopic hemostasis with metallic hemoclips for iatrogenic Mallory–Weiss tear caused by endoscopic examination. *Dig Endosc*. 2009;21:20–3.
14. Takizawa K, Oda I, Gotoda T, Yokoi C, Matsuda T, Saito Y, et al. Routine coagulation of visible vessels may prevent delayed bleeding after endoscopic submucosal dissection—an analysis of risk factors. *Endoscopy*. 2008;40:179–83.
15. Storey DW, Bowed SG, Swain CP, Salmon PR, Kirkham JS, Northfield TC. Endoscopic prediction of recurrent bleeding in peptic ulcers. *N Eng J Med*. 1981;305:915–6.
16. Jensen DM. Spots and clots—leave them or treat them? Why and how to treat. *Can J Gastroenterol*. 1999;13:413–5.
17. Sugiyama T, Dozaiku T, Toyonaga T, Hirooka T, Ueda C, Iwata Y, et al. The usefulness of 4 + 1 contact method using soft coagulation for bleeding gastric ulcers (in Japanese with English abstract). *Gastroenterol Endosc*. 2006;48:204–11.
18. Nagayama K, Tazawa J, Sakai Y, Miyasaka Y, Yu SH, Sakuma I, et al. Efficacy of endoscopic clipping for bleeding gastroduodenal ulcer: comparison with topical ethanol injection. *Am J Gastroenterol*. 1999;94:2897–901.
19. Chung IK, Ham JS, Kim HS, Park SH, Lee MH, Kim SJ. Comparison of the hemostatic efficacy of the endoscopic hemoclip method with hypertonic saline-epinephrine injection and a combination of the two for the management of bleeding peptic ulcers. *Gastrointest Endosc*. 1999;49:13–8.
20. Cipolletta L, Bianco MA, Marmo R, Rotondano G, Piscopo R, Vingiani AM, et al. Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomized trial. *Gastrointest Endosc*. 2001;53:147–51.
21. Waring JP, Sanowski RA, Sawyer RL, Woods CA, Foutch PG. A randomized comparison of multipolar electrocoagulation and injection sclerosis for the treatment of bleeding peptic ulcer. *Gastrointest Endosc*. 1991;37:295–8.
22. Lin HJ, Chan CY, Lee FY, Huang ZC, Lee CH, Lee SD. Endoscopic injection to arrest peptic ulcer hemorrhage: a prospective, randomized controlled trial; preliminary results. *Hepatogastroenterology*. 1991;38:291–4.
23. Loren L. Multipolar electrocoagulation versus injection therapy in the treatment of bleeding peptic ulcers. A prospective, randomized trial. *Gastroenterology*. 1990;99:1303–6.
24. Chung SCS, Leong HT, Chan ACW, Lau JY, Yung MY, Leung JW, et al. Epinephrine or epinephrine plus alcohol for injection of bleeding ulcers: a prospective randomized trial. *Gastrointest Endosc*. 1996;43:591–5.
25. Gralnek IM, Jensen DM, Gornbein J, Kovacs TO, Jutabha R, Freeman ML, et al. Clinical and economic outcomes of individuals with severe peptic ulcer hemorrhage and nonbleeding visible vessel: an analysis of two prospective clinical trials. *Am J Gastroenterol*. 1998;93:2009–11.
26. Sung JJ, Tsoi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermo-coagulation in the treatment of non-variceal upper gastrointestinal bleeding: a meta-analysis. *Gut*. 2007;56:1364–73.
27. Skok P, Krizman I, Skok M. Argon plasma coagulation versus injection sclerotherapy in peptic ulcer hemorrhage—a prospective, controlled study. *Hepatogastroenterology*. 2004;51:165–70.
28. Kanai M, Hamada A, Endo Y, Takeda Y, Yamakawa M, Nishikawa H, et al. Efficacy of argon plasma coagulation in nonvariceal upper gastrointestinal bleeding. *Endoscopy*. 2004;36:1085–8.
29. Andriulli A, Annese V, Caruso N, et al. Proton-pump inhibitors and outcome of endoscopic hemostasis in bleeding peptic ulcers: a series of meta-analyses. *Am J Gastroenterol*. 2005;100:207–19.
30. Yuan Y, Wang C, Hunt RH, Pilotto A, Accadia L, Niro AG, et al. Endoscopic clipping for acute nonvariceal upper-GI bleeding: a meta-analysis and critical appraisal of randomized controlled trials. *Gastrointest Endosc*. 2008;68:339–51.
31. Shimoda R, Iwakiri R, Sakata H, Ogata S, Kikkawa A, Ootani H, et al. Evaluation of endoscopic hemostasis with metallic hemoclips for bleeding gastric ulcer: comparison with endoscopic injection of absolute ethanol in a prospective, randomized study. *Am J Gastroenterol*. 2003;98:2198–202.
32. Raju GS, Gajula L. Endoclips for GI endoscopy. *Gastrointest Endosc*. 2004;59:267–79.
33. Gever AM, DeGoede E, Simoens M, Hiele M, Rutgeerts P. A randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. *Gastrointest Endosc*. 2002;55:466–9.
34. Nakayama M, Iwakiri R, Hara M, Ootani H, Shimoda R, Tsunada S, et al. Low-dose aspirin is a prominent cause of bleeding ulcers in patients who underwent emergency endoscopy. *J Gastroenterol*. 2009;44:912–8.