INTRODUCTION

In patients with acute upper gastrointestinal (UGI) bleeding, the bleeding site is by definition proximal to the ligament of Treitz and the patient presents with hematemesis or melena (1). The incidence of acute UGI bleeding is 50 to 150 per 100,000 of the population each year (2). UGI bleeding occurs in subjects of all ages, though this bleeding most often occurs in subjects 60 years and older and it has a male predominance (1). The overall mortality rate of UGI bleeding is approximately 14% (1).

The numerous advances in the medical management of UGI bleeding, including endoscopy, have significantly reduced the number of patients who require emergency surgical intervention for catastrophic bleeding (3, 4). Recently, endoscopy is often the first method used to investigate and treat UGI bleeding in patients with a visible vessel or active bleeding from peptic ulcers (5). However, the rate of re-bleeding or continued bleeding
after endoscopic treatment is approximately 15-20% (6, 7), mainly because of the technical difficulties or a case-based problem due to the presence of exposed arterial vessels, an ulcer with adherent clots, massive bleeding and a large ulcer with active bleeding.

The patients with UGI bleeding who continue to bleed after aggressive endoscopic treatment require invasive angiographic intervention. Transcatheter arterial embolization (TAE) has recently been successfully used for controlling bleeding that is detected by angiography in 95-100% of cases, with an overall clinical success rate of 76-91% (8-11). However, during angiography, it is relatively common (22-76%) that there is no detectable contrast medium extravasation (10-13), and this leads to difficulties in locating the exact site for embolization. This study evaluated the usefulness of rotational angiography after marking a bleeding site with a metallic clip during endoscopy in patients with no detectable extravasation of contrast medium seen on angiography.

MATERIALS AND METHODS

We obtained Institutional Review Board approval for the study and informed consent was waived. We retrospectively evaluated the clinical records of all consecutive patients who had confirmed acute UGI bleeding and who received angiography from January 2006 to September 2007. During this period, TAE for acute UGI bleeding was performed in 54 patients at our institution. Of these patients, 16 patients who failed to have their bleeding controlled via the endoscopic approach because a large amount of bleeding in the stomach underwent TAE without a metallic clip, and 11 patients of the 54 patients underwent TAE without the endoscopic approach. Twenty-seven patients underwent primary endoscopic treatment that included injection therapy, coagulation and/or the use of a metallic clip. The bleeding site was identified and endoscopic treatment was performed to stop the ongoing hemorrhage. However, none of the patients had undergone endoscopic treatment due to massive bleeding with large clots, large exposed vessels or large ulcerative lesions. Therefore, a metallic clip was placed in the fibrous edge of the ulcer adjacent to the bleeding point. All patients were immediately referred to the angiography suite for TAE. Of these patients, four patients did not undergo rotational angiography due to patients’ lack of cooperation and seven patients did not undergo rotational angiography due to visualization of the bleeding focus during the initial selective angiography. Therefore, 16 patients (M:F = 11:5; mean age, 59.4 years; age range, 34-82 years) with bleeding ulcers underwent marking with a metallic clip during endoscopy and rotational angiography. The cause of bleeding was a gastric ulcer in 13 patients, a duodenal ulcer in two patients and a malignant gastric ulcer in one patient.

A transfemoral approach was used in all cases with placement of a 6-Fr introducer (Radifocus; Terumo, Tokyo, Japan) into the common femoral artery. Celiac angiography was performed in each patient with the use of distal subtraction imaging (Artis dBA; Siemens, Erlangen, Germany) and selective arterial contrast injections with standard 5-Fr catheters (Radifocus; Terumo, Tokyo, Japan). When the bleeding site was not identified, selective angiography was performed with the use of a 3-Fr coaxial microcatheter system (Microferret; Cook, Bjaeverskov, Denmark) with a 0.016-inch guide wire (GT; Terumo, Tokyo, Japan) in the gastric artery and/or gastroduodenal artery. If the selective angiogram did not show any bleeding focus, then rotational angiography was performed to determine the relationship between the metallic clip and the branch of the gastric artery or gastroduodenal artery. For rotational angiography, the catheter tip was positioned in the location that was anticipated to be the bleeding focus of the gastric artery or gastroduodenal artery. A single series of rotational angiographic images were then obtained during a breath-hold by using the DynaCT technique, with one continuous C-arm rotation that covered 200° of a circular trajectory for approximately 8 seconds. With the use of a power injector, iodinated contrast medium (Visipaque 320; GE Healthcare, Princeton, NJ) was injected at a flow rate of 0.5-1.0 mL/sec for 8 seconds at the initiation of acquiring the DynaCT images, concurrent with the breath hold. The contrast medium was injected intraarterially directly into the microcatheter. The acquired images (240 images, frame rate, 24.8/sec; 0.8° of increment for each frame; resolution, 1024 pixels) were then transferred to a workstation (Leonardo; Siemens Medical Solutions).

After rotational angiography, we selected the frame between the suspected vessels and the metallic clip, and we performed superselective angiography. If the bleeding site was identified on superselective angiography, then embolization was performed with the use of microcoils (Cook, Bloomington, IN) or N-butyl cyanoacrylate (NBCA; Histoacryl, Braun, Melsungen, Germany) according to the location of the microcatheter around the bleeding focus.
Patients without detectable extravasation of contrast medium on a superselective angiogram after rotational angiography then underwent TAE with microcoils as close as possible to the clip. A check angiogram was performed after completion of each embolization procedure. Total occlusion of the feeding vessel without evidence of extravasation beyond the microcoils of contrast material or the NBCA-mixture was considered as the endpoint.

The data was analyzed according to the definitions and guidelines for percutaneous transcatheter embolization as determined by the Society of Interventional Radiology (14). Technical success was defined as an immediate cessation of bleeding as evaluated by completion angiography. Clinical success was defined as clinical cessation of bleeding and stabilization of the hemoglobin level, with a requirement of no more than two units of packed red blood cells after the procedure. Re-bleeding was assessed by checking the clinical parameters (passage of blood per rectum) and by hematological evaluation (a requirement of more than 2 units of packed red blood cells).

RESULTS

Table 1 summarizes all of the clinical results. All of the patients underwent rotational angiography during a single breath-hold by use of the DynaCT technique. A possible proximal branch, which was identified as close as possible to the metallic clip, arose from the left gastric artery (n = 11), right gastric artery (n = 2) and gastroduodenal artery (n = 3). Of the 16 patients, seven (44%) patients had active contrast medium extravasation detected on the superselective angiogram performed after rotational angiography in the stomach or duodenum and these seven patients underwent TAE with the use of microcoils (n = 5), NBCA (n = 1) or microcoils and NBCA (n = 1) (Fig. 1). Those patients who underwent TAE did not experience any re-bleeding.

Contrast extravasation was not detected on a superselective angiogram performed after rotational angiography in nine patients. Of these patients, two patients had a pseudaneurysm at the site of the metallic clip and these two patients underwent TAE with the use of microcoils (n = 2) (Fig. 2). One patient had an abrupt obstruction of a branch of the left gastric artery and the patient underwent TAE with the use of microcoils. Six patients without detectable contrast extravasation or indirect findings such as a vascular spot or vessel anomaly underwent TAE with the use of microcoils (n = 4) or gelfoam.

| No. | Gender | Age | Underlying Disease | Angiographic Findings | Feeding Artery | Embolic Material | Re-Bleeding | Follow-Up |
|-----|--------|-----|-------------------|-----------------------|--------------|-----------------|-------------|-----------|
| 1   | M      | 82  | Malignant GU      | Extravasation         | LGA          | NBCA            | -           | 4 weeks: cancer surgery |
| 2   | F      | 64  | GU                | Extravasation         | LGA          | Microcoil       | -           | Discharged |
| 3   | M      | 49  | GU, DM            | NS                    | LGA          | Gelfoam         | +*          | Discharged |
| 4   | M      | 34  | GU                | Extravasation         | RGA          | Microcoil       | -           | Discharged |
| 5   | F      | 57  | DU, LC            | NS                    | LGA          | Microcoil       | +           | Died: DIC |
| 6   | M      | 72  | GU                | Pseudoaneurysm        | LGA          | Microcoil       | -           | Discharged |
| 7   | F      | 68  | DU                | Extravasation         | RGA          | Microcoil       | -           | Discharged |
| 8   | F      | 59  | GU                | Extravasation         | GDA          | Microcoil       | -           | Discharged |
| 9   | M      | 70  | GU, DM            | Abrupt obstruction    | LGA          | Microcoil       | -           | Discharged |
| 10  | M      | 44  | GU                | NS                    | LGA          | Microcoil       | -           | Discharged |
| 11  | M      | 57  | GU, lung cancer   | NS                    | LGA          | Gelfoam         | -           | Discharged |
| 12  | M      | 51  | GU                | Pseudoaneurysm        | LGA          | Microcoil       | -           | Discharged |
| 13  | F      | 81  | GU, LC            | NS                    | LGA          | Microcoil       | -           | Discharged |
| 14  | M      | 42  | GU                | NS                    | GAD          | Microcoil       | -           | Discharged |
| 15  | M      | 55  | GU                | Extravasation         | GAD          | Microcoil       | -           | Discharged |
| 16  | M      | 69  | GU                | Extravasation         | LGA          | NBCA, microcoil | -           | Discharged |

Note. — *Repeated endoscopy and hemoclip. DIC = disseminated intravascular coagulation, DM = diabetes mellitus, DU = duodenal ulcer, F = female, GDA = gastroduodenal artery, GU = gastric ulcer, LC = liver cirrhosis, LGA = left gastric artery, M = male, NBCA = N-butylnbutyl cyanoacrylate, No. = number, NS = nonspecific findings, RGA = right gastric artery.
Fig. 1. 82-year-old man who presented with gastric ulcer with massive bleeding. 
A. Endoscopy shows large ulcer with multiple bleeding foci (arrows). Note metallic clip was placed in fibrous edge of ulcer. B. Left gastric artery angiography does not show any bleeding focus. C. After rotational angiography, superselective angiography that was done as close as possible to clip shows active contrast extravasation (arrow). D. Angiography after embolization with N-butyl cyanoacrylate does not show any evidence of bleeding. E. One-week follow-up endoscopy does not show red spot or presence of bleeding lesion.
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Fig. 2. 72-year old man with gastric ulcer and massive bleeding.
A. Endoscopy after placement of metallic clip in gastric ulcer shows small pseudoaneurysm adjacent to metallic clip (arrow).
B. Left gastric artery angiography does not show any bleeding focus.
C. After rotational angiography, superselective angiography as close as possible to clip shows presence of focal pseudoaneurysm (arrow).
D. Angiography after performing embolization with microcoils does not show any evidence of bleeding.
E. One-month follow-up endoscopy does not show pseudoaneurysm or gastric ulcer.
(n = 2) at a site as close as possible to the clip. Technical success, which was defined as target area devascularization, was achieved in 100% of the patients.

Of the six patients who received blind embolization without detectable contrast extravasation, two of these patients experienced a repeat episode of bleeding two days later, which required repeated endoscopic treatment. Of the two patients, one patient had subtle oozing at the ulcer margin and the patient underwent endoscopic treatment. One patient with a gastric ulcer continued to bleed with the hemoglobin level falling from 9 g/dL to 6 g/dL and the patient died due to disseminated intravascular coagulation one month after the embolization procedure. The remaining patients were clinically observed and they were discharged from the hospital after the return of stable vital signs and normal hematocrit levels. Therefore, complete clinical success was achieved in 14 of 16 (88%) patients.

There was no evidence of delayed bleeding or other major and minor complications related to embolization in all patients, excluding the one patient who died from the disseminated intravascular coagulation. Follow-up endoscopic evaluations were performed in ten patients one week later after embolization and postembolization complications such as ischemia or perforations were not observed in any of the patients.

DISCUSSION

Upper GI bleeding is typically intermittent and it ceases spontaneously. Localization of the bleeding site by angiographic evaluation requires that the patient is actively bleeding at the time of the study. Angiographically negative results are relatively common in patients with acute GI bleeding, and especially in patients with a stable hemodynamic status or lower GI bleeding. Most patients with a negative bleeding focus have experienced spontaneous resolution of their condition (15). But there remain some patients where an exhaustive investigational work-up fails to adequately identify a bleeding site, and these patients are subjected to repeat invasive investigations and blood transfusions. For localization of bleeding sites, performing provocative angiographic studies with the use of intraarterial tissue plasminogen activator (tPA), heparin, urokinase and tolazoline has been reported (16-19). Ryan et al. (19) reported that intraarterial provocative mesenteric angiography with the use of heparin, vasodilator and tPA identified the site of bleeding in 38% of patients and it contributed to treatment in 50% of patients. Although it is reasonably successful and without any reported hemorrhagic complications, provocative mesenteric angiography is not a commonly used examination due to potential hemorrhagic complications, it is a complex procedure and poor condition of patient. All of these previous studies were performed in patients with lower gastrointestinal (LGI) bleeding and they reported the positive results at the LGI tract, but not much is known about the clinical results of provocative angiography in patients with nonvariceal UGI bleeding.

In our hospital, endoscopy is the first step for making the diagnosis and managing UGI bleeding and the use of a metallic clip has been popular among our physicians to achieve endoscopic hemostasis. The applicator is inserted through the biopsy channel of the endoscope and the metallic clips are applied directly to the visible bleeding vessel. Some studies have reported a metallic clip to be effective (20, 21). However, the rate of re-bleeding or continued bleeding after endoscopic treatment is approximately 15-20% (6, 7) and this is mainly because of technical difficulties or case-based problems due to the presence of exposed arterial vessels, an ulcer with adherent clots, massive bleeding and a large ulcer with active bleeding.

In our hospital, none of the patients received endoscopic treatment due to the presence of massive bleeding with large clots, large exposed vessels or large ulcerative lesions. Therefore, a metallic clip was placed in the fibrous edge of the ulcer adjacent to the bleeding point. Eriksson et al. (22) reported that the embolization procedure benefited from marking with a clip in 60% of cases. However, although superselective angiography was performed as close as possible to the clip, most patients did not have detectable contrast extravasation or indirect signs of bleeding vessels, and they underwent TAE with the use of microcoils adjacent to the clip. In our study, direct contrast extravasation on the superselective angiography that was done after rotational angiography and using a metallic clip was seen in 44% (7 of 16) of the cases and indirect signs such as pseudoaneurysms or abrupt obstruction of an artery were seen in 19% (3 of 16) of the cases.

Three-dimensional (3D) rotational angiography can be considered to be superior to conventional planar angiography because it can provide multiple projections...
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with the use of only one injection of contrast medium. Although 3D rotational angiography has been one of the most commonly used interventional neuroradiology procedures, its use has also been applied to renal (23), uterine (24) and liver procedures (25-27). In previous studies, the use of conventional 3D rotational angiography helped to delineate complex vascular anatomy and this facilitated the subsequent delivery of a microcatheter to the target vessels. In our study, rotational angiography was performed to determine the relationship between the metallic clip and a branch of the gastric artery or gastroduodenal artery. After rotational angiography, the microcatheter was positioned as close as possible to the proximal branch and the metallic clip. A superselective angiogram of the proximal branch adjacent to the metallic clip showed active contrast medium extravasation in the stomach or duodenum in six patients. Therefore, TAE was performed for completely obstructing the bleeding vessels at the correct site.

There are some limitations to this study. First, we did not determine the effect of rotational angiography on the radiation exposure, the procedural time and the reduced load of contrast medium to the patient. Second, the patients with massive UGI bleeding and the older patients who were unable to perform a single-breath hold during rotational angiography were excluded from the study. Therefore, additional C-arm cone-beam CT was not used because of the possibility of poor imaging quality and respiratory artifacts. However, we only required information on the vascular anatomy between the metallic clip and bleeding vessels. Finally, the study was performed on a small subject population at a single tertiary-care academic medical center. Studies with a larger number of subjects need to be performed to firmly establish the protocol.

In conclusion, our results demonstrated that rotational angiography after marking with a metallic clip enhances the possibility that a bleeding focus is accurately localized and that the correct vessel is embolized. This procedure will most likely minimize the risk of recurrent bleeding after embolization. Prospective and preferably multicenter studies are needed to further refine the technique and to clinically validate the usefulness of the procedure.

REFERENCES

1. Rockall TA, Logan RF, Devlin HB, Northfield TC. Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. Steering Committee and members of the National Audit of Acute Upper Gastrointestinal Haemorrhage. BMJ 1995;311:222-226
2. Non-variceal upper gastrointestinal haemorrhage: guidelines. Gut 2002;51 Suppl 4:i1-6
3. Binmoeller KF, Thonke F, Soehendra N. Endoscopic hemoclip treatment for gastrointestinal bleeding. *Endoscopy* 1993;25:167-170
4. Saltzman JR, Strate LL, Di Sena V, Huang C, Merrifield B, Ookubo R, et al. Prospective trial of endoscopic clips versus combination therapy in upper GI bleeding (PROTECT-UGI bleeding). *Am J Gastroenterol* 2005;100:1503-1508
5. Longstreth GF. Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. *Am J Gastroenterol* 1995;90:206-210
6. Rupp T, Singh S, Waggenspack W. Gastrointestinal hemorrhage: The prehospital recognition, assessment & management of patients with a GI bleed. *JEMS* 2004;29:80-81, 83-95; quiz 96-87
7. Hung CF, Cheng TL, Wu RH, Teng CF, Chang WT. A novel bidirectional expression system for simultaneous expression of both the protein-coding genes and short hairpin RNAs in mammalian cells. *Biochem Biophys Res Commun* 2006;339:1035-1042
8. Aina R, Oliva VL, Therasse E, Pereaulet P, Bui BT, Dufresne MP, et al. Arterial embolotherapy for upper gastrointestinal hemorrhage: outcome assessment. *J Vasc Interv Radiol* 2001;12:195-200
9. Schenker MP, Duszak R Jr, Soulen MC, Smith KP, Baum RA, Cope C, et al. Upper gastrointestinal hemorrhage and transcatheter embolotherapy: clinical and technical factors impacting success and survival. *J Vasc Interv Radiol* 2001;12:1263-1271
10. Jae HJ, Chung JW, Jung AY, Lee W, Park JH. Transcatheter arterial embolization of nonvariceal upper gastrointestinal bleeding with N-butyl cyanoacrylate. *Korean J Radiol* 2007;8:48-56
11. Loffroy R, Rao P, Ota S, De Lin M, Kwak BK, Geschwind JF. Embolization of acute nonvariceal upper gastrointestinal hemorrhage resistant to endoscopic treatment: results and predictors of recurrent bleeding. *Cardiovasc Intervent Radiol* 2010;33:1088-1100
12. Hastings GS. Angiographic localization and transcatheter treatment of gastrointestinal bleeding. *Radiographics* 2000;20:1160-1168
13. Burke SJ, Golzarian J, Weldon D, Sun S. Nonvariceal upper gastrointestinal bleeding. *Eur Radiol* 2007;17:1714-1726
14. Drooz AT, Lewis CA, Allen TE, Citron SJ, Cole PE, Freeman NJ, et al. Quality improvement guidelines for percutaneous transcatheter embolization. SCVIR Standards of Practice Committee. Society of Cardiovascular & Interventional Radiology. *J Vasc Interv Radiol* 1997;8:889-895
15. Kim JH, Shin JH, Yoon HK, Chae EY, Myung SJ, Ko GY, et al. angiographically negative acute arterial upper and lower gastrointestinal bleeding: incidence, predictive factors, and
clinical outcomes. *Korean J Radiol* 2009;10:384-390
16. Malden ES, Hicks ME, Royal HD, Aliperti G, Allen BT, Picus D. Recurrent gastrointestinal bleeding: use of thrombolysis with anticoagulation in diagnosis. *Radiology* 1998;207:147-151
17. Bloomfeld RS, Smith TP, Schneider AM, Rockey DC. Provocative angiography in patients with gastrointestinal hemorrhage of obscure origin. *Am J Gastroenterol* 2000;95:2807-2812
18. Kim CY, Suhocki PV, Miller MJ Jr, Khan M, Janus G, Smith TP. Provocative mesenteric angiography for lower gastrointestinal hemorrhage: results from a single-institution study. *J Vasc Interv Radiol* 2010;21:477-483
19. Ryan JM, Key SM, Dumbleton SA, Smith TP. Nonlocalized lower gastrointestinal bleeding: provocative bleeding studies with intraarterial tPA, heparin, and tolazoline. *J Vasc Interv Radiol* 2001;12:1273-1277
20. 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;49:13-18
21. 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;53:147-151
22. Eriksson LG, Sundbom M, Gustavsson S, Nyman R. Endoscopic marking with a metallic clip facilitates transcatheter arterial embolization in upper peptic ulcer bleeding. *J Vasc Interv Radiol* 2006;17:959-964
23. Hagen G, Wadstrom J, Eriksson LG, Magnusson P, Magnusson M, Magnusson A. Three-dimensional rotational angiography of transplanted renal arteries: influence of an extended angle of rotation on beam-hardening artifacts. *Acta Radiol* 2005;46:170-176
24. Bucck RA, Reiter M, Dirisamer A, Kittenbach J, Lammer J. [Three-dimensional digital rotation angiography for embolization therapy of uterine leiomyomas: first results]. *Rofo* 2004;176:1001-1004
25. Tanigawa N, Komemushi A, Kojima H, Kariya S, Sawada S. Three-dimensional angiography using rotational digital subtraction angiography: usefulness in transarterial embolization of hepatic tumors. *Acta Radiol* 2004;45:602-607
26. Virmani S, Ryu RK, Sato KT, Lewandowski RJ, Kulik L, Mulcahy MF, et al. Effect of C-arm angiographic CT on transcatheter arterial chemoembolization of liver tumors. *J Vasc Interv Radiol* 2007;18:1305-1309
27. Kakeda S, Korogi Y, Ohnari N, Moriya J, Oda N, Nishino K, et al. Usefulness of cone-beam volume CT with flat panel detectors in conjunction with catheter angiography for transcatheter arterial embolization. *J Vasc Interv Radiol* 2007;18:1508-1516