

ORIGINAL ARTICLES—ALIMENTARY TRACT

Arterial Embolotherapy for Endoscopically Unmanageable Acute Gastroduodenal Hemorrhage: Predictors of Early Rebleeding

ROMARIC LOFFROY,* BORIS GUIU,* PHILIPPE D'ATHIS,[†] LISE MEZZETTA,* ALICE GAGNAIRE,[§] JEAN-LOUIS JOUVE,[§] PABLO ORTEGA-DEBALLON,^{||} NICOLAS CHEYNEL,^{||} JEAN-PIERRE CERCUEIL,* and DENIS KRAUSÉ*

*Department of Interventional Radiology and Endovascular Therapy, [†]Department of Medical Informatics and Biostatistics, [§]Department of Gastroenterology and Hepatology, ^{||}Department of Abdominal and Oncological Surgery, University of Dijon School of Medicine, Bocage Teaching Hospital, Dijon, France

See related article, Blitstein MK et al, on page xxvi in this issue of *CGH*.

Background & Aims: Severe bleeding from gastrointestinal ulcers is a life-threatening event that is difficult to manage when endoscopic treatment fails. Transcatheter embolization has been proposed but factors that influence the angiographic outcome are not well documented. We aimed to identify predictors of recurrent bleeding within 30 days after transcatheter embolization for refractory hemorrhage from gastroduodenal ulcers. **Methods:** This retrospective single-center study of 60 consecutive emergency embolization procedures included hemodynamically unstable patients (41 men, 19 women; mean age, 69.4 ± 15 y), referred from 1999 to 2008 for selective angiography after failed endoscopic treatment. Predictors of early rebleeding were tested with univariate analysis and a multivariate logistic regression model. **Results:** The procedural success rate was 95%, the primary clinical success rate was 71.9% (41 of 57), and secondary clinical success was achieved in 3 patients (77.2%) after repeat embolization. No major catheterization-related complications occurred. Periprocedural mortality was 26.7% (16 of 60). Early bleeding recurrence was associated with coagulation disorders ($P = .007$), longer time to angiography ($P = .0005$), greater preprocedural blood transfusion volume ($P = .0009$), 2 or more comorbidities ($P = .005$), and use of only coils ($P = .003$). Two factors were independent predictors of embolization failure: coagulation disorders (odds ratio, 6.18; $P = .027$) and the use of coils as the only embolic agent (odds ratio, 6.24; $P = .022$). The median follow-up time was 7 months (range, 1 day to 103 months). **Conclusions:** Angiographic embolization should be performed early in the course of bleeding, and not with coils alone, in critically ill patients. It is important to correct coagulation disorders throughout the embolization procedure.

Acute bleeding is the most common complication of peptic ulcer disease, and about half the cases of upper gastrointestinal bleeding are caused by gastric and duodenal ulcers.^{1,2} The mortality rate in patients with bleeding peptic ulcers remains as high as 5% to 10% and has failed to decrease substantially over the past 2 decades.³⁻⁵ Bleeding stops spontaneously

in 80% of cases and recurs or persists in 20%.^{1,5-7} Severe bleeding despite conservative medical treatment or endoscopic intervention occurs in 5% of patients,⁸ requiring surgery or transcatheter arterial embolization. A high surgical risk related to severe comorbidities is common, and surgical mortality rates of up to 40% have been reported.⁹ Endovascular management was introduced recently in many institutions as a less hazardous alternative to surgery and is now the first-line treatment for massive gastroduodenal bleeding refractory to endoscopic treatment.¹⁰⁻¹² However, in most of the published case series, no tests were performed to identify factors predicting angiographic and embolization failure, and the small numbers of patients limit the statistical validity of the results.

The aims of this study were to evaluate arterial embolotherapy for the treatment of severe, refractory, acute hemorrhage from gastroduodenal ulcers, and to identify factors associated with embolization outcomes and with rebleeding within 30 days.

Materials and Methods

Patient Selection

We retrospectively reviewed the medical records of all patients who underwent angiographic embolization for refractory bleeding from gastroduodenal ulcers from October 1999 to January 2008 at our institution. Patients were identified using the database maintained prospectively by our Interventional Radiology Department. Patients with hemobilia or bleeding from varices, malignancies, or traumatic lesions were excluded. We identified 63 angiographic embolization procedures in 60 consecutive patients with massive persistent or recurrent bleeding (defined as a need for more than 4 U of blood/24 h) causing hemodynamic instability (defined as clinical hypovolemic shock requiring volume replacement) despite initial conservative medical therapy and endoscopic treatment with local epinephrine injections or placement of metallic clips around the bleeding site. Reasons for interventional radiology referral before surgical intervention were poor surgical risk, patient or family refusal to consent to surgery, nondiagnostic previous upper

Abbreviations used in this paper: GDA, gastroduodenal artery; OR, odds ratio.

© 2009 by the AGA Institute
1542-3565/09/\$36.00
doi:10.1016/j.cgh.2009.02.003

endoscopy, or endoscopist's decision before surgical consultation. The mean time from hypovolemic shock onset to referral was 2.3 days (range, 12 hours to 8 days). This retrospective study was performed in compliance with the requirements of our institutional review board. Informed consent was not required.

Embolization Technique

All angiographic procedures were performed by 1 of 3 experienced interventional radiologists (R.L., J.-P.C., D.K.) with standard percutaneous transfemoral catheterization using a 5-F or 6-F sheath. Selective opacification of the celiac trunk and superior mesenteric artery was performed routinely using a 5-F Simmons-type catheter (Cook, Bjaaevskov, Denmark), followed by superselective arteriography (of the left gastric or gastroduodenal artery) using a 2.9-F co-axial microcatheter (Progreat; Terumo, Leuven, Belgium) if necessary. In 38 patients, extravasation of contrast medium or a false aneurysm-like lesion was seen at the bleeding site. Embolic therapy was performed as selectively as possible in 35 of these patients. In 3

patients, the right (2 patients) or left (1 patient) gastric artery was identified as the bleeding vessel but was too thin and tortuous to allow catheterization: no embolization was performed. In the 22 patients with no identifiable bleeding site, blind embolization was performed based on conclusive endoscopic examinations with identification of the source of bleeding, with the technique being at the discretion of the interventional radiologist. The left gastroepiploic artery was embolized through the splenic artery in 2 cases (Figure 1), and the left gastric artery selectively was occluded in 6 cases (Figure 2). Overall, embolization involved the gastroduodenal artery (GDA) and its branches or the pancreaticoduodenal arches in 49 patients, of whom 15 underwent selective embolization of the bleeding branch and 34 underwent embolization of the GDA trunk on either side of the bleeding site (known as the *sandwich technique*) (Figure 3), as previously reported.¹¹ In these 34 patients, the anterior and posterior superior pancreaticoduodenal arteries routinely were embolized; in 3 of these 34 patients, the anterior and posterior inferior pancreaticoduodenal arteries also selectively were embolized through the superior

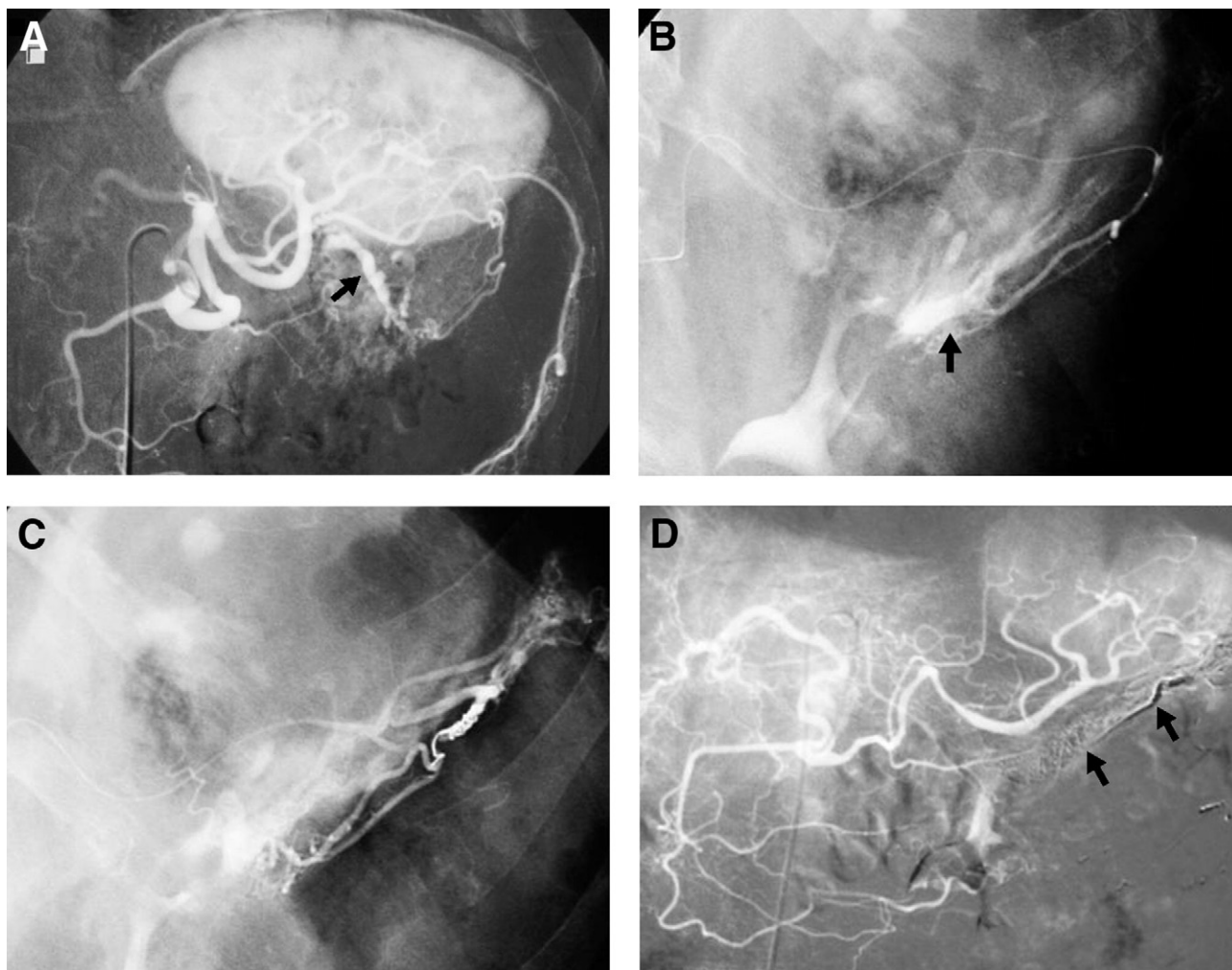


Figure 1. A 68-year-old man with massive hematemesis. (A and B) Selective angiography showed a bleeding ulcer in the gastric fundus, with extravasation of contrast medium from a branch of the left gastroepiploic artery (arrows). (C and D) The control angiogram after coil embolization throughout the splenic artery showed complete and selective occlusion of the bleeding branch, with no active bleeding (D, arrows). The patient was discharged from the hospital 6 days later.

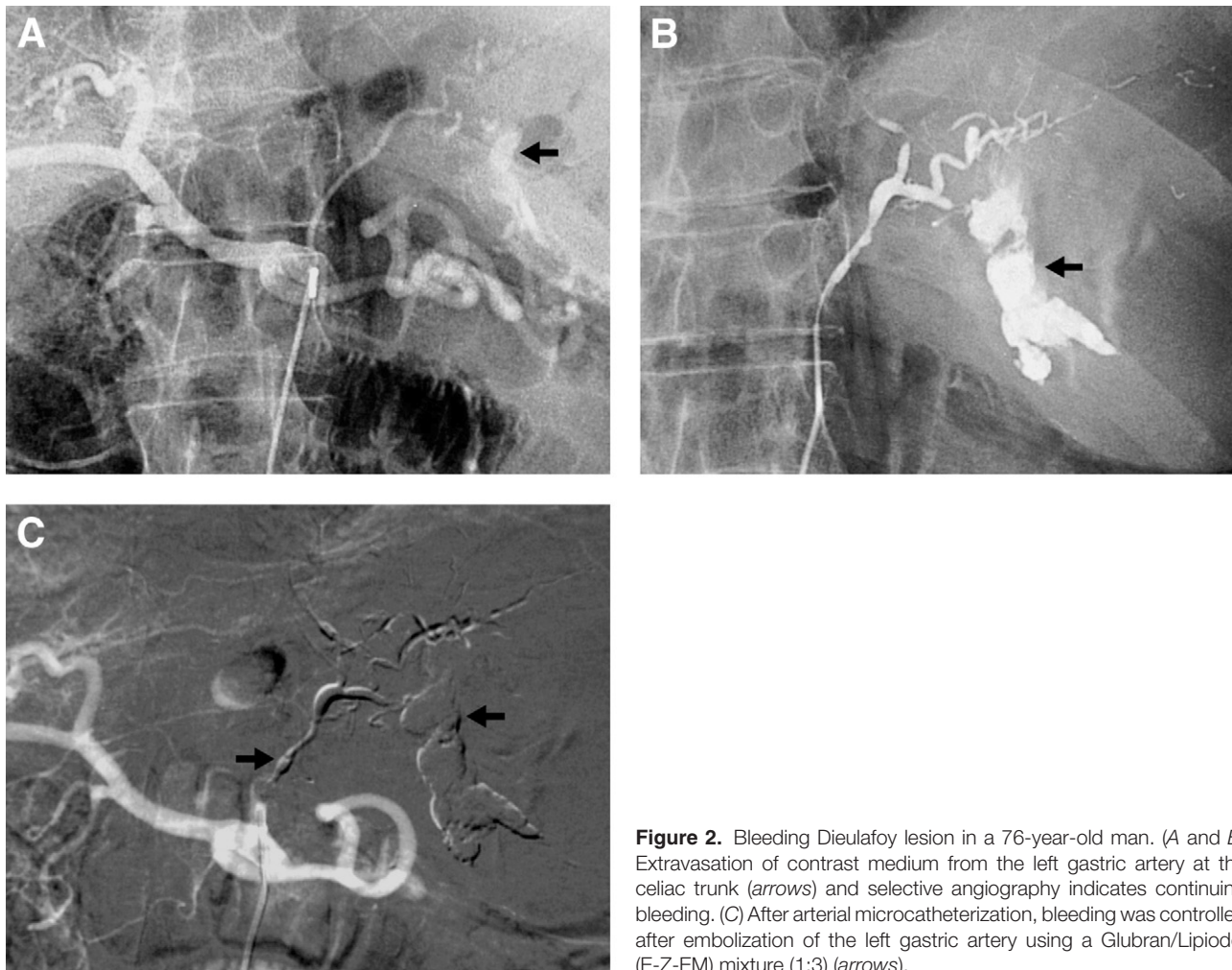


Figure 2. Bleeding Dieulafoy lesion in a 76-year-old man. (A and B) Extravasation of contrast medium from the left gastric artery at the celiac trunk (arrows) and selective angiography indicates continuing bleeding. (C) After arterial microcatheterization, bleeding was controlled after embolization of the left gastric artery using a Glubran/Lipiodol (E-Z-EM) mixture (1:3) (arrows).

mesenteric artery because of persistent extravasation. Embolization techniques according to arterial territories and angiographic findings are summarized in Figure 4. Embolization usually was achieved at the discretion of the intervention radiologist using coils (0.035-inch steel coils in the sandwich method or 0.018-inch soft platinum multiple-curved microcoils in the superselective method; Cook), a mechanically disrupted gelatin powder sheet (Curaspon; CuraMedical, Amsterdam, The Netherlands), or cyanoacrylate surgical glue (Glubran; GEM SRL, Viareggio, Italy) mixed with ultrafluid lipiodol (Therapex; E-Z-EM, Montreal, Canada) in a 1:3 ratio. In a few patients, 500- to 700- μ microspheres (EmboGold; Biosphere Medical, Roissy Ch De Gaulle, France) were used. In 28 patients, a single material was used (coils, 15; glue, 8; gelatin, 3; or microspheres, 2). In 13 patients, both coils and gelatin sponge were used to occlude the GDA: coils were released distally to prevent retrograde filling through the right gastroepiploic artery, gelatin sponge was placed in the arterial trunk, and additional coils were released in the proximal GDA. Coils and glue were used in 9 patients, gelatin sponge and microspheres were used in 3 patients, glue and gelatin were used in 1 patient, and coils and microspheres were used in 1 patient. In 2 patients, 3 embolic agents were used in combination.

The embolic agents used are listed in Table 1. All agents were released near the bleeding site until cessation of angiographic extravasation and/or occlusion of the targeted vessel as shown by fluoroscopic monitoring. The mean amount of contrast medium used was 190 mL (range, 120–290 mL) per patient and the mean total procedure time was 70 minutes (range, 50–105 min).

Collected Data and Follow-Up Evaluation

Follow-up information was available for all 60 patients. A physical examination was performed during the hospital stay and 1 month after hospital discharge as part of routine patient care. Data on subsequent events were collected during telephone interviews of patients and their usual physicians. The following variables were collected from medical records: patient demographics, comorbid conditions, prior coagulopathy (international normalized ratio, partial thromboplastin time, and platelet count), anti-inflammatory medication use, transfusion requirements, endoscopic and angiographic findings, vessel(s) embolized, embolic material used, complications, procedural and clinical outcomes, and mortality. The mean hospital length of stay was 18 days (range, 1–98 d) after embolization. The median follow-up period was 7 months (range, 1 day to 103 months).

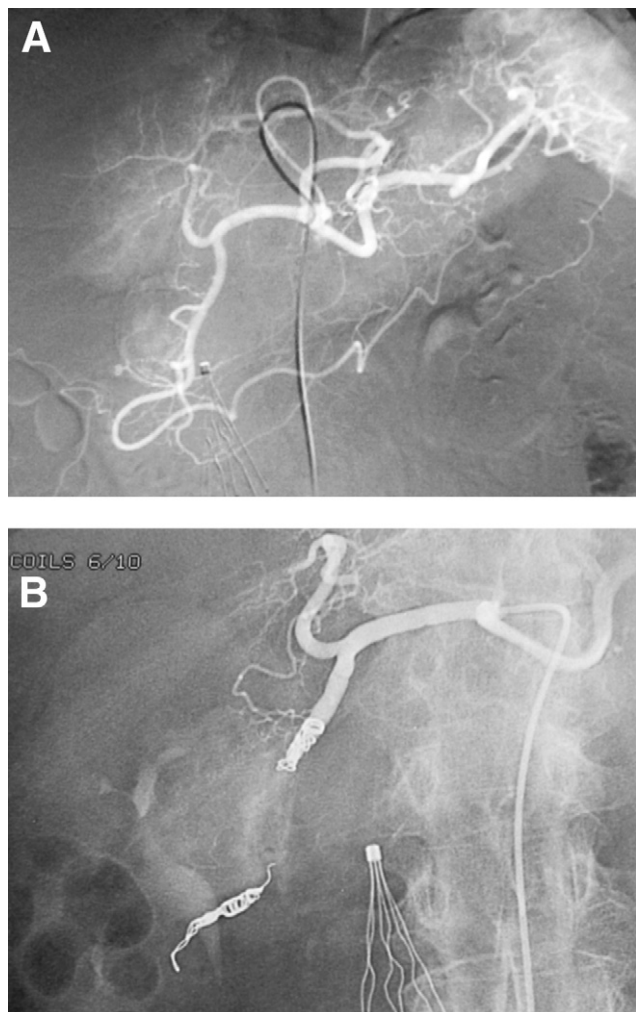


Figure 3. Typical sandwich embolization in a 76-year-old woman with bleeding from a post-bulbar duodenal ulcer at endoscopy. (A) Angiography before embolization: no evidence of active bleeding. (B) Result after coil embolization of the distal and proximal gastroduodenal artery, including the anterior and posterior superior pancreaticoduodenal arteries and the right gastroepiploic artery to prevent retrograde flow. No ischemic complications were reported.

Statistical Analysis

We investigated whether early rebleeding was associated with any of the following variables: age, sex, prior coagulopathy, anti-inflammatory drugs, number of comorbidities, time to angiography from initial bleeding, number of endoscopies, prior transfusion requirements, duodenal bleeding, angiographic extravasation, type of embolic agent, type of embolization, and death. For the univariate analysis, continuous variables were expressed as means (\pm SD) or medians (interquartile range) and compared using the Mann-Whitney *U* test, whereas categorical variables were expressed as the number (percentage) and compared between groups using the chi-square test or the Fisher exact test as appropriate. A further analysis using the Mantel-Hanszel test was performed to identify linking factors that were associated with early rebleeding in the coagulopathy group. Variables with *P* values less than .10 by univariate analysis were included in a multivariate logistic regression model to identify factors that

were associated independently with early rebleeding. Statistical analyses were performed using Triomphe software (Gex-Fabry, New York, NY)¹³ and STATA software (Stata Corporation, College Station, TX). In all analyses, *P* values less than .05 were considered significant.

Definitions

Procedural success was defined as the cessation of extravasation on the postembolization arteriography, primary clinical success as the absence of rebleeding within 1 month after a single embolization procedure, and secondary clinical success as the absence of rebleeding after attempted repeat embolization. Rebleeding was defined as bleeding with a greater than 2.0 g/dL decrease in the hemoglobin level and/or a lack of effectiveness of conservative medical treatment. Rebleeding events were classified as early events if they occurred within 30 days of embolization and as late events otherwise. Complications were classified as major complications if they required surgery and/or prolonged hospitalization (\geq 2 wk) and as minor complications otherwise. Patients who met one of the following criteria were classified in the coagulopathy group: international normalized ratio greater than 1.5, partial thromboplastin time longer than 45 seconds, or platelet count less than 80,000/mm³.

Results

Patient Characteristics

We reviewed 63 consecutive embolization procedures in 60 patients. There were 41 men and 19 women with a mean age of 69.4 years (range, 29–95 y). Most of the patients had a high surgical risk related to advanced age and comorbidities. Thus, 61.7% (37 of 60) of patients were older than 70 years, 38.3% (23 of 60) were older than 75 years, and 23.3% (14 of 60) were older than 80 years. Of the 60 patients, 54 (90%) had at least one serious comorbid condition and 25 (42%) had at least 2 comorbid conditions (Table 2). Furthermore, 48.3% (29 of 60) of patients had coagulation disorders as previously defined and 21.7% (13 of 60) were taking anti-inflammatory medications at hospital admission. All 60 patients underwent emergency endoscopy (mean, 1.6; range, 1–4), which identified gastric or duodenal peptic ulcers with signs of active bleeding (type 1, 33 patients), recent bleeding (type 2, 22 patients), or no bleeding (type 3, 5 patients) according to the classification of Forrest et al.¹⁴ The mean number of units of packed red blood cells used before embolization was 11 (range, 2–40), and the mean hemoglobin level at admission was 6.5 g/dL (range, 3–10.7 g/dL).

Technical Outcome

Endoscopy showed a bleeding peptic ulcer in 55 of the 60 patients (91.7%). The ulcer was located in the stomach in 9 patients, the bulbar duodenum in 35 patients, and the post-bulbar duodenum in 11 patients. In the 5 remaining patients (8.3%), the bleeding was from a Dieulafoy lesion in the fundus. Endovascular treatment was feasible in 57 of the 60 patients, for a 95% technical success rate (Table 3). In 3 patients, the bleeding vessel, which was the right (2 patients) or left (1 patient) gastric artery, was too slender and tortuous to allow catheterization; these 3 patients were treated successfully by surgery. In 17 patients, superselective embolization of the bleeding vessel was performed. In the remaining 22 patients, no extravasation was identified by angiography but the artery sup-

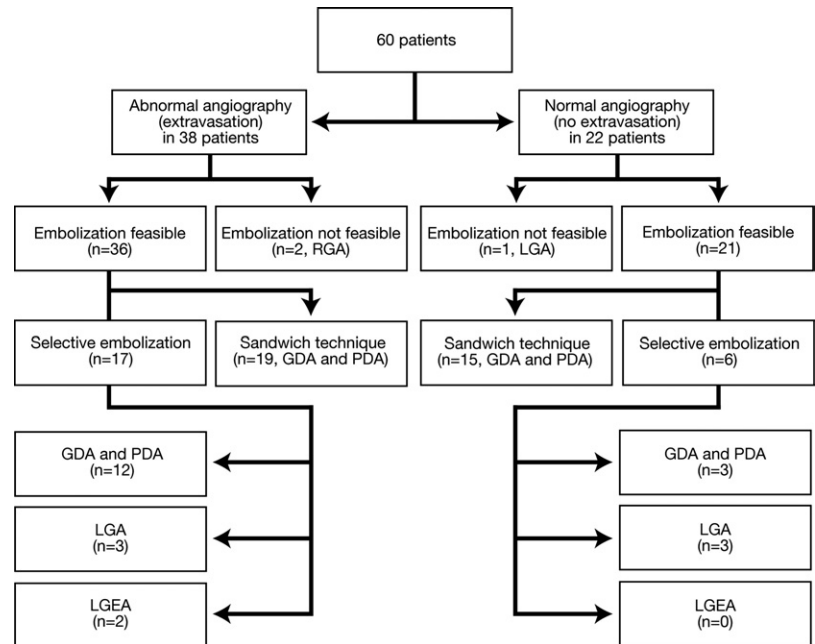


Figure 4. Summary of angiographic findings and arterial occlusion methods according to the embolized vessel. PDA, pancreaticoduodenal arteries; LGA, left gastric artery; LGEA, left gastroepiploic artery; RGA, right gastric artery.

plying the endoscopically identified bleeding site was embolized: in 3 patients, the left gastric artery was occluded using resorbable or nonresorbable particles, and in 19 patients the GDA was treated using the sandwich technique (15 patients) or selective embolization (4 patients). The vessels embolized in the entire series are summarized in Figure 4.

Clinical Outcome

Cessation of bleeding was achieved in 41 of 57 patients after the first embolization procedure, for a primary clinical success rate of 71.9% (Table 3). However, 16 patients required further treatment within the first 72 hours for recurrent bleeding: 8 patients were managed endoscopically, 3 patients initially treated by sandwich occlusion of the GDA underwent successful embolization of the inferior pancreaticoduodenal artery for a secondary clinical success rate of 77.2%, and 5 patients underwent surgery for duodenotomy. The second treatment ini-

tially was successful in all 16 patients, but 3 patients died after experiencing early rebleeding. Of the 57 patients treated with embolization, 16 (28.1%) died within 1 month after the procedure of the following causes: multiple organ failure (7 patients), hypovolemic shock caused by massive rebleeding (3 patients), pulmonary embolism (2 patients), septicemia (2 patients), malignancy (1 patient), and myocardial infarction (1 patient). None of the deaths was caused by ischemic complications. No significant rebleeding occurred after the first month. Eleven additional patients died during the follow-up evaluation of causes unrelated to the procedure, including underlying malignancy (5 patients), malnutrition (3 patients), septicemia (2 patients), and cardiorespiratory failure (1 patient).

Predictors of Early Rebleeding

Successfully treated patients were compared with the other patients (Tables 4 and 5). By univariate analysis, early

Table 1. Embolic Agents Used for Transcatheter Embolization in 57 Patients With Bleeding Gastroduodenal Ulcers

Embolic agents	Number (%) of patients
Embolic agents used in combination	29 (50.9)
Coils + gelatin sponge	13 (22.8)
Coils + cyanoacrylate	9 (15.8)
Gelatin sponge + microspherical particles	3 (5.3)
Coils + microspherical particles	1 (1.75)
Gelatin sponge + cyanoacrylate	1 (1.75)
Coils + cyanoacrylate + gelatin sponge	1 (1.75)
Coils + cyanoacrylate + microspherical particles	1 (1.75)
Embolic agents used alone	28 (49.1)
Coils	15 (26.3)
Cyanoacrylate	8 (14)
Gelatin sponge	3 (5.3)
Microspherical particles	2 (3.5)

Table 2. Comorbidities in 60 Patients With Bleeding Gastroduodenal Ulcers

Comorbidities	Number (%) of patients
Malignancy	21 (35)
Coronary heart disease	19 (31.7)
Pulmonary embolism/respiratory failure	18 (30)
Hypertension	15 (25)
Severe diabetes mellitus	14 (23.3)
Heart failure	12 (20)
Chronic renal failure	11 (18.3)
Cardiac arrhythmia	10 (16.7)
Stroke within the past 15 days	7 (11.7)
Peripheral occlusive arterial disease	6 (10)
Surgery within the past 15 days	4 (6.7)
Cirrhosis	3 (5)

NOTE. Most patients were at high surgical risk because of comorbid conditions. The total is greater than 60 (100%) because most patients had more than one comorbid condition.

Table 3. Outcomes After Embolization

	Number of patients	Percentage
Procedural success	57/60	95
Primary clinical success	41/57	71.9
Secondary clinical success	44/57	77.2
Rebleeding		
Early rebleeding (<30 d)	16/57	28.1
Late rebleeding (>30 d)	0/57	0
Complications ^a		
Major complications	2/60	3.3
Minor complications	4/60	6.7
Mortality rate		
Time		
Within 1 mo	16/60	26.7
After 1 mo	11/44	25
Cause		
Recurrent bleeding	3/27	11.1
Underlying illness	24/27	88.9

^aComplications were classified as major if they required surgery and/or prolonged hospitalization (≥ 2 wk) and as minor otherwise.

rebleeding was associated with coagulation disorders ($P = .007$), a longer time from shock onset to angiography (3.9 vs 1.8 d; $P = .0005$), a larger number of red-blood-cell units transfused before angiography (15.9 vs 8.9 U; $P = .0009$), having 2 or more comorbid conditions ($P = .005$), and being treated with coils as the only embolic agent ($P = .003$). Factors associated independently with early rebleeding in the multivariate analysis were the presence of a coagulation disorder (odds ratio [OR], 6.18; 95% confidence interval, 1.23–30.97; $P = .027$) and the use of coils as the only embolic agent (OR, 6.24; 95% confidence interval, 1.29–30.05; $P = .022$). Comorbid conditions (≥ 2), which often were present in patients who had coagulation disorders, were not identified as a predictor of rebleeding in the multivariate analysis because of intercorrela-

Table 4. Univariate Analysis: Predictors of Clinical Outcome Within 30 Days of Embolization

Variable	Clinical success (n = 41)	Clinical failure (n = 16)	P value
Age, y	70.1 \pm 15.7	69.2 \pm 12.6	.545
Male sex	28 (68.3%)	11 (68.7%)	.999
Prior coagulopathy ^a	16 (32%)	13 (81.2%)	.007
Anti-inflammatory drugs ^b	8 (19.5%)	5 (31.2%)	.483
≥ 2 comorbidities	22 (53.6%)	15 (93.7%)	.005
Days to angiography	1.8 \pm 1.5	3.9 \pm 1.7	.0005
Number of endoscopies	1.6 \pm 0.81	2 \pm 0.82	.334
Prior packed red blood cells	8.9 \pm 6.3	15.9 \pm 8.1	.0009
Coils alone	6 (14.6%)	9 (56.2%)	.003
Duodenal bleeding	33 (80.5%)	15 (93.7%)	.268
Angiographic extravasation	28 (68.3%)	8 (50%)	.232
Selective embolization	19 (46.3%)	4 (25%)	.229
Number of deaths	9 (21.9%)	6 (37.5%)	.316

NOTE. Data are means \pm SD or n (%). $P < .05$.

^aInternational normalized ratio >1.5 or partial thromboplastin time >45 seconds, or platelet count $<80,000/\text{mm}^3$.

^bNonsteroidal anti-inflammatory drugs or corticosteroids.

Table 5. Multivariate Analysis: Factors Associated Independently With Rebleeding Within 30 Days of Embolization

Variable	Odds ratio	95% CI	P value
Coagulopathy ^a	6.18	1.23–30.97	.027
Coils alone	6.24	1.29–30.05	.022
≥ 2 comorbidities	6.49	0.71–59.13	.097

NOTE. Variables with P values less than .10 by univariate analysis were included in the multivariate model. $P < .05$.

CI, confidence interval.

^aInternational normalized ratio >1.5 or partial thromboplastin time >45 seconds, or platelet count $<80,000/\text{mm}^3$.

tion between these 2 factors. In addition, the presence of coagulopathy was associated with rebleeding within 30 days, specifically in patients with 2 or more comorbidities ($P = .011$), or in whom the number of days to angiography was greater than 2 ($P = .031$). In other words, patients with more than 2 comorbid conditions or in whom time to angiography was longer than 2 days were at higher risk for early rebleeding if they had coagulation disorders. Early rebleeding was not predicted by age, sex, anti-inflammatory drugs, number of endoscopies before angiography, duodenal source of bleeding, extravasation at angiography, selective embolization, or death.

Complications

No major complications related to embolization were reported. There were 4 minor complications. In a patient with proximal celiac trunk occlusion and retrograde filling of the GDA through the inferior pancreaticoduodenal artery, catheterization beyond the bleeding site was not feasible, and retrograde occlusion of the inferior pancreaticoduodenal artery, GDA, and common hepatic artery was achieved using resorbable particles (after verification of portal venous flow). The liver enzyme activities increased in this patient and then returned to normal within a few days. Another patient had a transient increase in serum amylase levels without symptoms. In the last 2 patients, a microcoil migrated into the common hepatic artery during embolization; this event had no detectable effects. Two major angiography-related complications were recorded. In 1 patient, a hematoma in the groin area and hemodynamic instability developed, requiring vascular surgery. In the other patient, who was obese (160 kg), a false aneurysm of the femoral artery was identified a few days after the procedure but produced no symptoms; thrombosis was achieved by 20 minutes of mechanical compression under Doppler sonography guidance. No ischemic gastrointestinal complications were identified by clinical examination.

Discussion

Although sonography has been used as a diagnostic tool, with visualization of an intragastric clot being taken as evidence of bleeding,¹⁵ endoscopy remains the first-line method for diagnosing and treating actively bleeding peptic ulcers because its success rate is high. Recent advances in endoscopic hemostasis techniques ensure bleeding control in most patients. Endoscopic treatment is particularly valuable in patients whose advanced age or comorbid conditions pose a high surgical risk. When endoscopy fails, surgery is associated with

mortality rates as high as 20% to 40%.^{9,16} Therefore, endovascular embolization has generated interest as an alternative to surgery in high-risk patients with bleeding despite endoscopic treatment. The use of endovascular embolization is supported by the high technical and primary clinical success rates in our study (95% and 71.9%, respectively). However, factors influencing the clinical outcome, especially predictors of early rebleeding, are poorly understood, and few studies have addressed this issue. Most of the studies reported to date included small numbers of patients and failed to separate peptic ulcers from other causes of bleeding such as malignant tumors, vascular malformations, trauma-induced lesions, and postinflammatory lesions.¹⁷ We confined our study to patients who had gastric or duodenal peptic ulcers (55 patients) or Dieulafoy lesions (5 patients). Endoscopy was successful in identifying the bleeding site in all our patients. Endoscopic findings are valuable to the interventional radiologist for determining the artery that requires occlusion because extravasation of contrast medium may not be visualized on the global arteriogram. De Wispelaere et al¹⁸ showed extravasation by celiac arteriography in only 11 (39%) of 28 patients with bleeding duodenal ulcers. We obtained a higher rate of 38 (63.3%) among 60 patients, probably because we injected both the celiac trunk and the GDA, followed by the superior mesenteric artery. However, our study shows that embolization can be performed successfully even when angiography fails to visualize extravasation of contrast medium. In our series, active bleeding was present in 38 (63.3%) of the 60 patients and did not predict the outcome of embolotherapy. Several previous studies^{11,19-21} found that empiric embolization based on endoscopic findings, in the absence of contrast extravasation, was helpful in achieving bleeding control, with no difference according to whether angiography identified the bleeding site. In our series, outcomes were not different between patients who underwent blind embolization and those who underwent embolization after angiographic visualization of the bleeding site.

In our study, 2 factors independently predicted embolization failure by multivariate analysis, namely, the presence of a coagulation disorder (OR, 6.18; $P = .027$) and the use of coils as the only embolic agents (OR, 6.24; $P = .022$). Coagulopathy has been reported to increase the clinical failure rates of percutaneous embolization (OR, 2.9-19.6).^{11,20-22} The association between coagulopathy and rebleeding was confirmed with the finding of a strong statistical significance in our series. These data emphasize the need for correcting coagulation disorders before, during, and after embolization for upper gastrointestinal hemorrhage. In addition, the presence of more than 2 comorbidities and time to angiography longer than 2 days were associated with rebleeding in the univariate analysis, specifically in patients with coagulation disorders. Thus, the ability to achieve bleeding control in critically ill patients seems to depend chiefly on early intervention and on the severity of the underlying disease. Even if comorbid conditions was not identified as a predictor of rebleeding in the multivariate analysis because of intercorrelation with coagulopathy, recurrence of bleeding was associated with comorbidities in the univariate analysis, and probably depends on the clinical setting and whether or not the patient has the ability to clot. Although 21.9% of successfully treated patients died within 30 days of embolization versus 37.5% of unsuccessfully treated patients ($P = .316$), their deaths were related mainly to underlying disease, as

opposed to ongoing bleeding. A possible explanation is that patients were stabilized after a first embolization procedure despite being considered a clinical failure, thereby allowing time to reorient the treatment strategy and ultimately result in success. Aina et al²⁰ reported a periprocedural mortality rate of 34.6% (26 of 75), with most deaths being caused by underlying diseases, namely, cirrhosis and malignancy. Severe hypovolemic shock at admission, advanced age, and comorbidities probably contributed to the 26.7% one-month mortality rate in our study, which simply reflected the high surgical risk in our population. Only 3 deaths were caused by early rebleeding.

The influence of the type of embolic agent on clinical outcomes is more controversial. In most of the previous series,²²⁻²⁶ the number of patients was too small to allow conclusions about choosing the embolic agent. However, Aina et al²⁰ reported that using coils only predicted embolization failure by multivariate analysis. Similarly, in our study, using coils as the only embolic agent ($P = .003$) independently predicted a poor clinical outcome. These data support combining coils with a gelatin sponge, cyanoacrylate, or microspherical particles for the treatment of gastroduodenal hemorrhage, especially with the sandwich technique, but there is no consensus in the literature on the choice of embolic agent.

Of the 16 rebleeding events in our study, 15 occurred after embolization of the GDA and its branches. The abundant collateral circulation in the duodenum probably explains this finding. No cases of rebleeding occurred in the 6 patients in whom surgical glue was used alone for selective embolization of the left gastric artery (4 patients) or left gastroepiploic artery (2 patients). Two factors that may have contributed to this good result are the scantier collateral circulation in this territory and the more selective and more distal character of arterial occlusion obtained with glue. In previous studies, embolization produced a higher success rate in patients with gastric rather than duodenal ulcers, presumably because the left gastric artery supplies 85% of gastric bleeds.^{27,28} However, the use of n-butyl cyanoacrylate glue requires considerable experience, given the risk of gastric infarction and glue reflux into other vessels. The use of glue is very interesting, however, in hemodynamically unstable patients, because it provides faster hemostasis than other embolic agents.²⁵

Ripoll et al²⁹ reported the only retrospective study comparing outcomes of embolization (31 patients) or surgery (39 patients) after failed endoscopic treatment for bleeding peptic ulcers. No differences were found between the 2 groups for the incidence of rebleeding, need for additional surgery, or death, although the embolotherapy group included significantly older patients with more comorbidities, such as heart disease and prior anticoagulation therapy. Unfortunately, the postprocedural morbidity rate was not compared between the 2 techniques.

Few investigators have reported data on postsurgical morbidity, most notably complications related to the surgical method and infectious complications. The postsurgical morbidity rate was 45% in a study by Cheynel et al.⁹ In our study, no cases of bowel ischemia occurred. In addition, major complications developed in only 3.3% of patients and were unrelated to vascular occlusion. The main complications were puncture-site injuries, which perhaps could be decreased by using small introducers and catheters (4-F), delayed introducer retrieval (within 24 hours) after normalization of the coagulation pa-

rameters, or vascular closure devices. The low postoperative morbidity rate is one of the main advantages of embolization over surgery. In the long term, duodenal stenosis was the most troublesome complication (25%) in a study of 28 patients followed up for at least 5 years after embolization for bleeding duodenal ulcers.²³ No cases of clinically symptomatic duodenal stenosis occurred during follow-up evaluation in our population, even in the patients treated with surgical glue, probably because the follow-up period was too short. However, a more aggressive investigation strategy might have detected asymptomatic cases. The link between embolization and duodenal stenosis is difficult to evaluate because duodenal stenosis can occur as a complication of peptic ulcer disease. None of our patients experienced significant rebleeding requiring endoscopy or invasive treatment during the median 7-month follow-up period. Thus, embolization was effective not only in controlling the acute bleeding episode, but also in preventing late recurrences.

A weakness of the present study was its retrospective nature, with a short clinical follow-up period. There is clearly a need for prospective, randomized, controlled studies comparing surgical and endovascular management of massive gastrointestinal tract bleeding after endoscopic failure, and also comparing the different embolic agents used when endovascular therapy is performed, although such studies would be difficult to perform in the emergency setting.

In summary, our experience suggests that arterial embolization in well-trained hands is effective in controlling bleeding from gastroduodenal ulcers, even when extravasation is not visualized by angiography, and does not cause ischemia. In our institution, this technique is now the salvage treatment of choice after failure of endoscopic treatment. In most cases, embolization obviates the need for surgery. Every effort should be made to perform embolization early after bleeding onset and to correct coagulation disorders. In addition, careful selection of the embolic agents according to the bleeding vessel is essential for a successful outcome; specifically, coils probably should not be used as the only embolic agent, but in association with gelatin sponge, particles, or glue. Finally, treatment decisions must be made jointly by gastroenterologists, interventional radiologists, and surgeons.

References

- Laine L, Peterson WL. Bleeding peptic ulcer. *N Engl J Med* 1994; 331:717-727.
- National Institutes of Health Consensus Conference. Therapeutic endoscopy and bleeding ulcers. *JAMA* 1989;262:1369-1372.
- Goldman ML, Land WC, Bradley EL, et al. Transcatheter therapeutic embolization in the management of massive upper gastrointestinal bleeding. *Radiology* 1976;120:513-521.
- Dousset B, Suc B, Boudet MJ, et al. Surgical treatment of severe ulcerous hemorrhages: predictive factors of operative mortality. *Gastroenterol Clin Biol* 1995;19:259-265.
- Rollhauser C, Fleischer DE. Nonvariceal upper gastrointestinal bleeding: an update. *Endoscopy* 1997;29:91-105.
- Alexander S, Nathan DM, Korman MG. Outcome of peptic ulcer bleeding. *Clin Gastroenterol Hepatol* 2006;4:661.
- Targownik LE, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993-2003. *Clin Gastroenterol Hepatol* 2006;4:1459-1466.e1.
- Qvist P, Arnesen KE, Jacobsen CD, et al. Endoscopic treatment and restrictive surgical policy in the management of peptic ulcer bleeding: five year's experience in a central hospital. *Scand J Gastroenterol* 1994;29:569-576.
- Cheyne N, Peschaud F, Hagry O, et al. Bleeding peptic ulcer: results of surgical management. *Ann Chir* 2001;126:232-235.
- Loffroy R, Guiu B, Cercueil JP, et al. Refractory bleeding from gastroduodenal ulcers: arterial embolization in high-operative-risk patients. *J Clin Gastroenterol* 2008;42:361-367.
- Poultides GA, Kim CJ, Orlando R 3rd, et al. Angiographic embolization for gastroduodenal hemorrhage: safety, efficacy, and predictors of outcome. *Arch Surg* 2008;143:457-461.
- Larssen L, Moger T, Bjornbeth BA, et al. Transcatheter arterial embolization in the management of bleeding duodenal ulcers: a 5.5-year retrospective study of treatment and outcome. *Scand J Gastroenterol* 2008;43:217-222.
- Gex-Fabry M, Balant LP. Consideration on data analysis using computer methods and currently available software for personal computers. In: Welling P, Balant H, eds. *Handbook of experimental pharmacology*. Volume 110. Pharmacokinetics of drugs. New York: Springer, 1994.
- Forrest JAH, Finlayson NDC, Scheerman DJC. Endoscopy of upper gastrointestinal bleeding. *Lancet* 1974;2:394-397.
- Farin P, Janatuinen E. Sonographic detection of intragastric blood clot. *Eur Radiol* 1997;7:262-263.
- Vellakot KD, Dronfield MW, Atkinson M, et al. Comparison of surgical and medical management of bleeding peptic ulcers. *Br J Med* 1982;284:548-550.
- Krämer SC, Görlich J, Rilinger N, et al. Embolization for gastrointestinal hemorrhages. *Eur Radiol* 2000;10:802-805.
- De Wispelaere JF, De Ronde T, Trigaux JP, et al. Duodenal ulcer hemorrhage treated by embolization: results in 28 patients. *Acta Gastroenterol Belg* 2002;65:6-11.
- Walsh RM, Anain P, Geisinger M, et al. Role of angiography and embolization for massive gastroduodenal hemorrhage. *J Gastrointest Surg* 1999;3:61-66.
- Aina R, Oliva VL, Therasse E, et al. Arterial embolotherapy for upper gastrointestinal hemorrhage: outcome assessment. *J Vasc Interv Radiol* 2001;12:195-200.
- Schenker MP, Duszak R Jr, Soulen MC, et al. Upper gastrointestinal hemorrhage and transcatheter embolotherapy: clinical and technical factors impacting success and survival. *J Vasc Interv Radiol* 2001;12:1263-1271.
- Encarnacion CE, Kadir S, Beam CA, et al. Gastrointestinal bleeding: treatment with gastrointestinal arterial embolization. *Radiology* 1992;183:505-508.
- Lang EK. Transcatheter embolization in management of hemorrhage from duodenal ulcer: long-term results and complications. *Radiology* 1992;182:703-707.
- Toyoda H, Nakano S, Takeda I, et al. Transcatheter arterial embolization for massive bleeding from duodenal ulcers not controlled by endoscopic hemostasis. *Endoscopy* 1995;27:304-307.
- Toyoda H, Nakano S, Kumada T, et al. Estimation of usefulness of N-butyl-2-cyanoacrylate-lipiodol mixture in transcatheter arterial embolization for urgent control of life-threatening massive bleeding from gastric or duodenal ulcer. *J Gastroenterol Hepatol* 1996;11:252-258.
- Morris DC, Nichols DM, Connell DG, et al. Embolization of the left gastric artery in the absence of angiographic extravasation. *Cardiovasc Intervent Radiol* 1986;9:195-198.
- Kelemouridis V, Athanasoulis C, Waltman A. Gastric bleeding sites: an angiographic study. *Radiology* 1983;149:643-648.
- Kerlan RK, Pogany AC, Burke DR, et al. Angiographic management of upper gastrointestinal hemorrhage. *AJR Am J Roentgenol* 1986;147:1185-1188.
- Ripoll C, Banares R, Beceiro I, et al. Comparison of transcatheter arterial embolization and surgery for treatment of bleeding peptic

ulcer after endoscopic treatment failure. *J Vasc Interv Radiol* 2004;15:447-450.

Dijon School of Medicine, Bocage Teaching Hospital, 2 bd du Maréchal de Lattre de Tassigny, BP 77908, 21079 Dijon Cedex, France. e-mail: romaric.loffroy@chu-dijon.fr; fax: (33) 380-293-243.

Reprint requests

Address requests for reprints to: Romaric Loffroy, MD, Department of Interventional Radiology and Endovascular Therapy, University of

Conflicts of interest

The authors disclose no conflicts.