

# Angiographic Embolization for Gastroduodenal Hemorrhage

## Safety, Efficacy, and Predictors of Outcome

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**Objective:** To examine the safety, efficacy, and predictors of outcome of angiographic embolization in the management of gastroduodenal hemorrhage.

**Design:** Retrospective record review.

**Setting:** University-affiliated tertiary care center.

**Patients:** All of the patients were referred after endoscopic treatment failure. Surgery was not immediately considered because of poor surgical risk, refusal to consent, or endoscopist's decision. Patients with coagulopathy, hemobilia, and variceal or traumatic upper gastrointestinal tract bleeding were excluded from review.

**Interventions:** Between January 1, 1996, and December 31, 2006, 70 embolization procedures were performed in 57 patients.

**Main Outcome Measures:** Technical success rate (target vessel devascularization), clinical success rate (in-hospital cessation of bleeding without further endoscopic, radiologic, or surgical intervention), and complications.

**Results:** The technical success rate was 94% (66 of 70 angiographies). The primary clinical success rate was 51% (29 of 57 patients), and the clinical success rate after repeat embolization was 56% (32 of 57 patients). Two factors were found to be independent predictors of poor outcome by multivariate analysis: recent duodenal ulcer suture ligation ( $P=.03$ ) and blood transfusion of more than 6 units prior to the procedure ( $P=.04$ ). There was no predictive value for angiographic failure based on age, sex, prior coagulopathy, renal failure at presentation, immunocompromised status, multiple organ system failure, empirical (blind) embolization, and use of permanent vs temporary embolic agents. Repeat embolizations were helpful for postsphincterotomy bleeding. Major ischemic complications (4 patients [7%]) were associated with previous foregut surgery.

**Conclusions:** Angiographic embolization for gastroduodenal hemorrhage was associated with in-hospital rebleeding in almost half of the patients. Angiographic failure can be predicted if embolization is performed late, following blood transfusion of more than 6 units, or for rehemorrhage from a previously suture-ligated duodenal ulcer.

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**A**CUTE UPPER GASTROINTESTINAL (GI) tract bleeding will stop spontaneously in approximately 80% of patients. In patients with persistent bleeding, therapeutic endoscopy can achieve hemostasis in almost 80% of cases.<sup>1</sup> Surgical intervention is usually an expeditious and gratifying endeavor required in fewer than 5% of patients with

zation is now considered the first-line therapy for colonic hemorrhage<sup>4,5</sup> and hemobilia,<sup>6</sup> the safety and durability of this modality for upper GI tract bleeding remains unclear. This study will attempt to define the role of angiographic embolization for gastroduodenal hemorrhage and to identify factors that could predict angiographic failure so as not to delay operative intervention.

## See Invited Critique at end of article

upper GI tract hemorrhage but can be associated with operative mortality rates of up to 30% in patients with severe comorbidity.<sup>2,3</sup> Although angiographic emboli-

## METHODS

### PATIENTS

All of the patients who underwent angiographic embolization for upper GI tract bleeding from January 1, 1996, to December 31, 2006, at Hartford Hospital, Hartford, Connecticut,

were identified using a prospectively maintained interventional radiology database. Patients with persistent coagulopathy, hemobilia, and variceal or traumatic bleeding were excluded. Seventy angiographic embolization procedures in 57 consecutive patients were retrospectively reviewed. Data collection included patient demographics, diagnosis, comorbid conditions, steroid use or other immunosuppression, prior coagulopathy, renal failure at presentation, transfusion requirements, multiple organ system failure, vessel(s) embolized, type of embolic agent(s) used, incidence of empirical or blind embolizations, incidence of complications (gastric or duodenal ischemia, inadvertent spleen or liver embolization, superior mesenteric artery dissection, nephrotoxicity, groin hematoma), clinical outcome, and mortality.

Coagulopathy was defined as an international normalized ratio higher than 1.5, a partial thromboplastin time longer than 45 seconds, or a platelet count of less than 50 000/mL.<sup>7</sup> The technical success rate was defined as target vessel devascularization. The clinical success rate was defined as in-hospital cessation of bleeding without further endoscopic, radiologic, or surgical intervention. The secondary clinical success rate after repeat angiographic embolization was also analyzed.

## INTERVENTIONS

All of the patients had persistent or recurrent bleeding despite initial therapy consisting of volume replacement, correction of coagulopathy, intravenous administration of H<sub>2</sub> receptor blockers or proton pump inhibitors, and at least 1 previous attempt to control the bleeding by endoscopic means. Reasons for interventional radiology referral before surgical intervention were poor surgical risk, patient or family refusal to consent to surgery, nondiagnostic previous upper endoscopy, or endoscopist's decision prior to surgical consultation. Sodium bicarbonate infusion was instituted in patients at high risk for contrast nephrotoxicity.<sup>8</sup>

Angiographic procedures were performed with standard percutaneous transfemoral catheterization using a 5- or 6-French sheath. All of the patients had selective opacification of the celiac trunk and superior mesenteric artery, followed by superselective arteriography of the left gastric artery or gastroduodenal artery as necessary. Images were obtained with the digital subtraction technique. When extravasation of contrast material was demonstrated at angiography, embolic therapy was performed as selectively as possible, with a 3-French Tracker microcatheter (Target Therapeutics, Fremont, California) coaxially inserted through the 5-French catheter into the target vessel. The embolic agents used were temporary, such as cellulose sponge plugs (Gelfoam; Pharmacia and Upjohn, Kalamazoo, Michigan); permanent, such as vascular coils ranging from 2 to 7 mm (Gianturco; Cook, Bloomington, Indiana), platinum microcoils (Target Therapeutics), and 355- to 500- $\mu$ m or 500- to 710- $\mu$ m polyvinyl alcohol particles (Contour; Target Therapeutics); or a combination of both. If direct entry into the bleeding artery was not possible, occlusion was attempted by means of a flow-directed injection of the embolic agent. When a dual blood supply existed, contrast injection through the alternate route was performed to exclude extravasation by retrograde filling. If this was demonstrated, embolization through the second limb was carried out until cessation of extravasation was achieved.

In certain patients without angiographic evidence of contrast extravasation into the gastroduodenal lumen or other vascular anomaly, such as a pseudoaneurysm, neovascularity, or arteriovenous malformation, empirical or blind embolization was achieved based on conclusive endoscopic identification of the source of bleeding. Pharmacocoarteriography with the use of anticoagulants, vasodilators, or fibrinolytic agents to provoke contrast medium extravasation was not performed.

## STATISTICAL ANALYSIS

The  $\chi^2$  test and Fisher exact test, where appropriate, were used for univariate comparisons. Binary logistic regression was used to incorporate all of the explanatory variables in a model predicting clinical success. Statistical analysis was performed using SPSS version 11.0 statistical software (SPSS, Inc, Chicago, Illinois) for Windows (Microsoft Corp, Redmond, Washington).  $P < .05$  was considered statistically significant.

## RESULTS

### PATIENT CHARACTERISTICS

A total of 70 consecutive embolization procedures were reviewed in 57 patients. There were 38 men (67%). The mean age was 65 years (range, 22-93 years).

Diagnoses were duodenal ulcer ( $n=13$ ), postsphincterotomy bleeding ( $n=10$ ), gastric ulcer ( $n=8$ ), gastric cancer ( $n=5$ ), duodenal ulcer previously suture ligated ( $n=5$ ), Mallory-Weiss tear ( $n=4$ ), Dieulafoy lesion ( $n=3$ ), duodenal arteriovenous malformation ( $n=2$ ), periampullary neoplasm ( $n=2$ ), arterial-duodenal fistulas (inferior pancreaticoduodenal artery pseudoaneurysm secondary to pancreatitis [ $n=2$ ] and aberrant right hepatic artery pseudoaneurysm following hepatic artery infusion pump placement [ $n=1$ ]), duodenal vasculitis ( $n=1$ ), and cytomegalovirus duodenitis ( $n=1$ ).

Comorbid conditions noted were steroid use or other immunosuppression ( $n=14$  [25%]), prior coagulopathy ( $n=15$  [26%]), renal failure at presentation ( $n=15$  [26%]), transfusion requirement of more than 6 units of packed red blood cells prior to the procedure ( $n=27$  [47%]), and multiple organ system failure ( $n=15$  [26%]).

### PROCEDURAL OUTCOMES

Embolization was technically possible in 66 of 70 angiographies, reaching a technical success rate of 94%. Technical failures were mainly associated with stenosis of the celiac trunk, which precluded superselective catheterization, or inability to safely occlude the targeted vessel without inadvertent splenic, hepatic, or superior mesenteric artery embolization.

Arteries primarily embolized were the gastroduodenal artery ( $n=30$ ), the left gastric artery ( $n=18$ ), the inferior pancreaticoduodenal artery ( $n=10$ ), an aberrant right hepatic artery ( $n=4$ ), the right gastroepiploic artery ( $n=2$ ), the splenic artery ( $n=1$ ), and the superior pancreaticoduodenal artery ( $n=1$ ). In 3 duodenal ulcer cases, the gastroduodenal artery was successfully embolized but superior mesenteric arteriography revealed back bleeding from the inferior pancreaticoduodenal artery; the inferior pancreaticoduodenal artery was subsequently embolized, achieving angiographic hemostasis. In 1 case of bleeding gastroesophageal junction carcinoma, left gastric artery occlusion was supplemented with embolization of a left inferior phrenic perforator to the tumor to accomplish cessation of contrast extravasation.

Empirical embolizations were performed in 22 patients (39%), and permanent embolic agents were used in 33 of the 66 technically successful embolization procedures.

**Table 1. Univariate and Multivariate Predictors of Embolization Failure**

Predictor	Patients, No. (%) (N=57)	Univariate Analysis		Logistic Regression Analysis	
		P Value	OR (95% CI)	P Value	
Age >70 y	26 (46)	.32	0.59 (0.13-2.53)	.48	
Male	38 (67)	.13	2.53 (0.63-10.08)	.18	
Duodenal ulcer after suture ligation	5 (9)	.11	0.24 (0.07-0.78)	.03	
Prior coagulopathy	15 (26)	.43	7.27 (0.95-55.51)	.05	
Immunosuppression	14 (25)	.40	1.40 (0.17-11.08)	.74	
Renal failure at presentation	15 (26)	.06	0.25 (0.03-1.82)	.17	
MOSF	15 (26)	.15	0.09 (0.01-1.26)	.07	
> 6 U of PRBCs prior to procedure	27 (47)	.02	0.25 (0.06-0.95)	.04	
Permanent embolic agents	29 (51)	.73	0.35 (0.07-1.69)	.19	
Empirical embolization	22 (39)	.45	1.92 (0.47-7.72)	.35	

Abbreviations: CI, confidence interval; MOSF, multiple organ system failure; OR, odds ratio; PRBCs, packed red blood cells.

## CLINICAL OUTCOMES

In-hospital cessation of bleeding without further endoscopic, radiologic, or surgical intervention was accomplished in 29 of 57 patients (51%). The primary clinical success rate was higher for duodenal ulcer (8 of 13 patients [62%]) and gastric cancer (3 of 5 patients [60%]). The mean interval to rebleeding in the 28 primary failures was 3.8 days (range, 1-22 days). Thirteen patients underwent repeat embolization. Three of them eventually achieved hemostasis, with a secondary clinical success rate of 56% (32 of 57 patients). Repeat embolization was successful in 2 cases of postsphincterotomy bleeding and 1 case of duodenal arteriovenous malformation.

Rebleeding occurred in 25 patients (44%) despite initial or repeat embolization. Eleven of those patients underwent surgery, and 8 recovered well. Three patients died in the postoperative period, 2 from duodenal stump blow-out following salvage antrectomy after failed gastroduodenal artery embolization for a bleeding duodenal ulcer and 1 secondary to gastric remnant necrosis following salvage distal subtotal gastrectomy after unsuccessful left gastric artery embolization for a bleeding gastric ulcer. Of the remaining 14 patients with angiographic failures, 8 were salvaged with repeat endoscopy and 6 died secondary to bleeding or underlying terminal disease. Mortality was 36% (9 of 25 patients) when embolization failed and 9% (3 of 32 patients) when embolization was successful. Overall mortality was 21% (12 of 57 patients).

Seven angiographic embolizations were performed in 5 patients with recurrent bleeding from a previously suture-ligated duodenal ulcer. Bleeding recurred in all but 1 case of an embolized gastroduodenal artery pseudoaneurysm. Of the remaining 4 cases of angiographic failure, 2 patients were salvaged with antrectomy and 2 patients died as described earlier.

## COMPLICATIONS

Four patients (7%) experienced major ischemic complications. Three of them resulted in postoperative deaths as described previously. The fourth complication was a liver abscess in an immunosuppressed patient after gastroduodenal artery embolization for postsphincter-

otomy bleeding. Eight patients (14%) experienced minor complications, including inadvertent spleen or liver embolization without clinical sequelae (n=3), groin hematoma (n=1), and transient perioperative renal insufficiency (n=4).

## PREDICTORS OF OUTCOME

Eight patient variables and 2 procedural variables were subjected to univariate and multivariate analysis to identify predictors of outcome (**Table 1**). By univariate analysis, a transfusion requirement of more than 6 units of blood prior to the procedure was the only variable found to be associated with clinical failure ( $P=.02$ ). Two factors were found to be independent predictors of embolization failure by multivariate analysis. Patients with recurrent bleeding from a previously suture-ligated duodenal ulcer had only a 24% likelihood of achieving long-term hemostasis with embolization (odds ratio=0.24; 95% confidence interval, 0.07-0.78;  $P=.03$ ) compared with patients with other diagnoses. Similarly, patients who received fewer than 6 units of blood prior to the procedure were 4 times more likely to have a clinically successful embolization (odds ratio=0.25; 95% confidence interval, 0.06-0.95;  $P=.04$ ). There was no predictive value for angiographic failure based on age, sex, prior coagulopathy, immunocompromised status, renal failure at presentation, multiple organ system failure, use of permanent vs temporary embolic agents, and empirical (blind) embolization.

## COMMENT

The first transcatheter embolization for upper GI tract bleeding was of the right gastroepiploic artery using autologous clot and was described by Röscher et al<sup>9</sup> in 1972. Embolotherapy for lower GI tract bleeding was reported at almost the same time but had an unacceptably high bowel ischemic rate and quickly fell out of favor.<sup>10</sup> Most believe such high rates were due to the availability of only large catheters and primitive embolic agents by today's standards. However, since the advent of microcatheters ( $\leq 3$  French) and associated embolics, superselective transcatheter embolization has become first-line therapy for co-

**Table 2. Published Series of Angiographic Embolization for Upper Gastrointestinal Tract Bleeding**

Source	Patients, No.	Technical Success Rate, %	Primary Clinical Success Rate, %	Empirical (Blind) Embolizations, %	Major Ischemic Complications, %	Mortality, %
Lieberman et al, <sup>11</sup> 1984	32	100	59	16	6	26
Dempsey et al, <sup>12</sup> 1990	34	NA	62	59	0	41
Encarnacion et al, <sup>13</sup> 1992	29	NA	62	NA	0	34
Lang, <sup>14</sup> 1992	57	91	40	NA	16	NA
Walsh et al, <sup>15</sup> 1999	50	92	52	50	2	40
Aina et al, <sup>16</sup> 2001	75	99	76	38	4	35
Schenker et al, <sup>17</sup> 2001	163	95	58	63	1	33
Defreyne et al, <sup>18</sup> 2001	20	95	68	33	5	32
Ljungdahl et al, <sup>19</sup> 2002	18	94	78	28	0	6
Ripoll et al, <sup>20</sup> 2004	31	94	65	NA	3	26
Holme et al, <sup>21</sup> 2006	40	95	65	70	0	25
Our study	57	94	51	39	7	21

Abbreviation: NA, not available.

ionic hemorrhage with rebleeding rates between 10% and 40%.<sup>4,5</sup> In contrast, angiographic embolization for upper GI tract bleeding has been largely limited to these rare situations where endoscopy is unsuccessful and surgery is not considered. Since 1984, there have been 11 articles on angiographic embolization for nonvariceal upper GI tract hemorrhage, consisting of 549 patients (**Table 2**).<sup>11-21</sup> There is a need to clearly define the efficacy, safety, and durability of this modality as well as the clinical criteria for the selection of patients who may benefit from it.

Unlike lower GI tract bleeding, angiographic confirmation of a bleeding site is not a prerequisite for transcatheter therapy in the upper GI tract. Although an early study by Dempsey et al<sup>12</sup> did not find empirical embolizations based on surgical or endoscopic guidance (without evidence of contrast extravasation) to be helpful in controlling hemorrhage, 3 succeeding studies showed no difference between patients with empirical embolization and patients with positive angiography results.<sup>15-17</sup> Lang et al,<sup>22</sup> describing 13 patients with massive upper GI tract hemorrhage and normal angiogram results, concluded that prophylactic embolization of the left gastric artery appears warranted when there is definite prior identification of a lesion in the left gastric artery territory or there is no prior localization of a lesion but the patient is at risk for multiple organ failure if bleeding recurs. In our series, empirical embolization was performed in 22 patients (39%) and was not found to independently predict angiographic failure, confirming the current practice of almost all centers to empirically embolize the most likely offending vessel based on endoscopic guidance.

Although not as worrisome as with lower GI tract embolotherapy, ischemia does occur following upper GI tract embolization. Despite the foregut's rich collateral blood supply, reported rates of major ischemic complications range from 0% to 16% (Table 2). Late ischemic complications can be more frequent with terminal vessel embolization, which has been associated with a 25% incidence of late duodenal stricture in 1 study.<sup>14</sup> Our study did not have the long-term endoscopic follow-up to confirm the incidence of this late complication. However, we did have 3 major ischemic complications, 2 involving the proximal stomach and 1 involving the duodenal stump, in the

setting of previous distal gastrectomy. Lieberman et al<sup>11</sup> reported 3 ischemic complications in their series of 32 patients embolized for upper GI tract bleeding, all of whom had surgically altered anatomy. This finding concurs with our observation that postembolization intestinal ischemia can be aggravated by previous gastric resection.

Predictors of clinical failure to control upper GI tract bleeding seem to agree that coagulopathy and multiple organ failure result in a reduced likelihood of clinical success. Schenker et al<sup>17</sup> found a 17.5-fold increased mortality rate in patients with multiple organ failure and upper GI tract bleeding. However, patients with multiple organ failure and successful embolization had a 69% rate of survival compared with a 4% rate of survival when embolization failed, prompting the investigators to conclude that embolization should be attempted in these patients despite their higher mortality rate. Coagulopathy has been shown to adversely affect the success rate for embolotherapy with an increase in the odds ratio for clinical failure, which ranges from 2.9 to 19.6.<sup>13,16,17</sup> Therefore, aggressive correction of coagulation parameters is our recommended institutional policy before embolization for GI tract bleeding. Walsh et al<sup>15</sup> found longer time to angiography ( $P = .01$ ), more total units of packed red blood cells ( $P = .003$ ), and prior surgery for bleeding ( $P = .02$ ) to be predictors of embolization failure by multivariate analysis. Our study agrees with the earlier findings, indicating that recent duodenal ulcer surgery ( $P = .03$ ) and blood transfusion of more than 6 units prior to the procedure ( $P = .04$ ) are independent predictors of poor embolization outcome.

To our knowledge, no studies have prospectively compared transcatheter therapy with other modalities in the management of gastroduodenal hemorrhage. Ripoll et al<sup>20</sup> attempted to retrospectively compare transcatheter embolotherapy for the treatment of bleeding peptic ulcers refractory to endoscopic intervention vs surgery. Although there was no difference between the embolotherapy and surgery groups in the incidence of recurrent bleeding (29% vs 23.1%, respectively), need for additional surgery (16.1% vs 30.8%, respectively), or mortality (25.8% vs 20.5%, respectively), the embolotherapy group included significantly older patients with more comorbidities, such as heart

disease and prior anticoagulation therapy. There is clearly a great need for prospective, randomized, controlled studies comparing surgical and endovascular management of massive GI tract bleeding after endoscopic failure, although this task would be intrinsically difficult to perform in the emergency setting.

In summary, angiographic embolization for nonvariceal upper GI tract hemorrhage is a viable option in poor candidates for surgery. When used, it should be performed with the understanding that despite initial technical success, bleeding can recur in almost half of the patients. Previous foregut surgery can exacerbate ischemic complications. Failure to achieve long-term hemostasis can be predicted if embolization is performed late in the course of bleeding following transfusion of more than 6 units of blood or in the setting of recurrent bleeding from a previously suture-ligated duodenal ulcer.

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## INVITED CRITIQUE

**P**oultides and colleagues conducted a retrospective review over a 10-year period of patients with uncontrolled upper GI tract hemorrhage who were treated with angiography and embolization. This highly selective group of 57 patients had significant comorbidities: one-quarter had multiple organ system failure; similar percentages had immunocompromise, renal failure, or coagulopathy. Remarkably, some patients were referred to angiography by consultants who chose not to obtain a surgical consultation.

What they found was not surprising. The initial success in controlling bleeding was 94%, but 44% of the patients rebled and there was only a 51% overall success rate. About half of the patients who failed ultimately needed surgery, and the overall mortality rate was 21%. Complications included ischemic bowel from the angiography or embolization.

Few studies have looked at prognostic indicators in patients as complicated as these. Using multivariate analysis, Poultides and colleagues nicely show that those pa-