Mesenteric angiography for acute gastrointestinal bleed: predictors of active extravasation and outcomes

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Background: Ongoing gastrointestinal bleeding (GIB) following endoscopic therapy and deciding between mesenteric angiography and surgery often challenge surgeons. We sought to identify predictors of positive angiographic study (active contrast medium extravasation) and characterize outcomes of embolization for acute GIB.

Methods: We retrospectively analyzed angiographies for GIB at 2 teaching hospitals from January 2005 to December 2008. The χ^2 , Wilcoxon rank sum and t tests determined significance. A Cox proportional hazards model was used for multivariate analyses.

Results: Eighteen of 83 (22%) patients had active extravasation on initial angiography and 25 (30%) were embolized. Patients with active extravasation had more packed red blood cell (PRBC; 5.3 v. 2.8 units, p < 0.001) and fresh frozen plasma (4.8 v. 1.7 units, p = 0.005) transfusions 24 hours preangiography and were more likely to be hemodynamically unstable at the time of the procedure (67% v. 28%, p = 0.001) than patients without active extravasation. Each unit of PRBC transfused increased the risk of a positive study by 30% (hazard ratio [HR] 1.3, 95% confidence interval [CI] 1.2–1.6 per unit). Embolization did not decrease recurrent bleeding (53% v. 52%) or length of stay in hospital (28.1 v. 27.5 d, p = 0.95), but was associated with a trend toward fewer emergency surgical interventions (13% v. 26%, p = 0.31) and greater 30-day mortality (33% v. 7%, p = 0.006) than nonembolization. Blind embolization was performed in 10 of 83 (12%) patients and was found to be an independent predictor of death in patients without active extravasation (HR 9.2, 95% CI 1.5–55.9).

Conclusion: The number of PRBC units transfused correlates with greater likelihood of a positive study. There was a significant increase in mortality in patients who underwent angioembolization. Large prospective studies are needed to further characterize the indications for angiography and blind embolization.

Contexte: En présence d'un saignement gastro-intestinal persistant après un traitement endoscopique, les chirurgiens hésitent souvent entre l'angiographie mésentérique et la chirurgie. Nous avons voulu dégager les prédicteurs d'un examen angiographique positif (extravasation active de l'agent de contraste) et caractériser les résultats de l'embolisation pour saignement gastro-intestinal aigu.

Méthodes: Nous avons effectué une analyse rétrospective des angiographies pour saignement gastro-intestinal dans 2 hôpitaux d'enseignement entre janvier 2005 et décembre 2008. Le χ^2 , le test de Wilcoxon et le test t ont permis d'en établir la portée. Nous avons utilisé un modèle de risques proportionnels de Cox pour les analyses multivariées.

Résultats: Dix-huit patients sur 83 (22 %) présentaient une extravasation active lors de l'angiographie initiale et 25 (30 %) ont subi un traitement d'embolisation. Les patients qui présentaient une extravasation active ont reçu plus de culots globulaires (5,3 unités c. 2,8, p < 0,001) et de plasma frais congelé (4,8 unités contre 1,7, p = 0,005) 24 heures avant l'angiographie et étaient plus susceptibles d'être stables au plan hémodynamique au moment de l'intervention, comparativement aux patients ne présentant pas d'extravasation active (67 % c. 28 %, p = 0,001). Chaque unité de culot globulaire transfusé a fait augmenter de 30 % le risque que les résultats de l'examen soient positifs (risque relatif [RR] 1,3, intervalle de confiance [IC] à 95 % 1,2–1,6 par unité). L'embolisation n'a pas réduit la récurrence des saignements (53 % c. 52 %) ni la durée du séjour hospitalier (28,1 j c. 27,5 j, p = 0,95), mais a été associée à une tendance à moins d'interventions urgentes (13 % c. 26 %, p = 0,31) et à une mortalité à 30 jours plus élevée que la non-embolisation (33 % c. 7 %, p = 0,006). L'embolisation à l'aveugle a

été réalisée chez 10 patients sur 83 (12 %) et s'est révélée être un prédicteur indépendant de mortalité en l'absence d'extravasation active (RR 9,2, IC à 95 % 1,5–55,9).

Conclusion : Le nombre d'unités de culots globulaires transfusés est en corrélation avec une probabilité plus grande de résultats positifs à l'examen. On a noté une augmentation significative de la mortalité chez les patients qui ont subi une angioembolisation. Il faudra procéder à des études prospectives de plus grande envergure pour compléter la caractérisation des indications de l'angiographie et de l'embolisation à l'aveugle.

cute gastrointestinal bleeding (GIB) is a common clinical problem that accounts for up to 2% of hospital admissions. Upper GIB (UGIB), defined as proximal to the ligament of Treitz, accounts for more than 80% of acute GIB. Lower GIB (LGIB) originates mainly from the colon, with diverticulosis and angiodysplasia accounting for most cases. 2

After initial hemodynamic resuscitation, emergent endoscopy is the initial treatment of choice for both acute UGIB³ and LGIB.⁴⁻⁶ However, the ideal management for ongoing bleeding after failure of endoscopic therapy remains controversial. Acute surgical intervention will eventually be required in 10%–15% of patients,⁷ but is associated with a mortality of 25%.⁸

Mesenteric angiography and angioembolization is a well described diagnostic and therapeutic option in the management of both acute UGIB⁹⁻¹² and LGIB¹³⁻¹⁶ after endoscopic failure. The decision to perform mesenteric angiography or proceed directly with surgical intervention is often at the discretion of the attending surgeon. Active contrast medium extravasation, which occurs in 24%–78% of patients, ^{17,18} can be visualized using angiography and treated with angioembolization; however, it is unclear which patients will have a positive angiogram. Therefore, we sought to identify the different predictors for a positive mesenteric angiogram and characterize the outcomes of angioembolization in the management of acute GIB.

METHODS

We identified all patients who underwent mesenteric angiography for acute nonvariceal UGIB or LGIB at 2 university-affiliated hospitals between January 2005 and December 2008. Patients who were transferred to another institution within 24 hours postangiography were excluded. These patients were transferred to our tertiary care institution for the sole purpose of mesenteric angiography, and subsequently were transferred back to the referring institution postprocedure. We included only the initial mesenteric angiography in our analysis.

The decision to use mesenteric angiography was made at the discretion of the treating physician, most of whom were intensivists or general surgeons. Esophagogastroduodenoscopy or lower gastrointestinal endoscopy was the initial diagnostic modality for both UGIB and LGIB. If a source of bleeding was identified, specific endoscopic interventions were performed depending on the pathology encountered. Mesenteric angiography was then performed when bleeding persisted despite previous endoscopic therapy. The attending interventional radiologist or the interventional radiology fellow performed all mesenteric angiographies. A positive angiogram was defined as the presence of active contrast medium extravasation or a visualized blush. The choice of embolization agent was also at the discretion of the attending interventional radiologist. Embolization agents included gelatin sponge particles, polyvinyl alcohol particles and metallic microcoils. Selective catheterization of the celiac trunk and superior mesenteric artery (SMA) was performed for acute UGIB, followed by super-selective catheterization of celiac and SMA branches, as indicated. Mesenteric angiography for LGIB was performed by selective catheterization of the SMA and inferior mesenteric artery (IMA), followed by superselective catheterization of SMA and IMA branches.

We compared the clinical and procedural variables of patients with active extravasation on initial mesenteric angiography with those of patients without active extravasation to identify predictors for a positive mesenteric angiogram. Outcomes of embolization were characterized by comparing patients who underwent embolization (excluding blind embolization) to those who did not. We defined therapeutic embolization as the cessation of active extravasation following embolization. Technical success was defined as the ability to perform embolization in the presence of active contrast medium extravasation. We considered bleeding to be recurrent if there was any evidence of GIB requiring additional invasive diagnostic and therapeutic interventions. We defined blind embolization as nonselective embolization in the absence of active contrast medium extravasation. The site of bleeding was initially localized via endoscopy in the blind embolization group, and the decision to perform blind embolization was made at the interventional radiologist's discretion, in consultation with either the endoscopist or the surgeon, after failure of endoscopic control. We compared outcomes of angioembolization in the presence of active contrast medium extravasation and blind angioembolization.

Statistical analysis

Data were entered and analyzed using SPSS version 16 (SPSS Inc.). The χ^2 , Wilcoxon rank sum and Student t

tests determined significance on univariate analysis. The Cox proportional hazards model was used for multivariate analysis. We considered results to be significant at p < 0.05.

RESULTS

A total of 83 patients who fit the study criteria were identified over a 3-year period (January 2005 to December 2008). There were 55 men (66%) and 28 women (34%) with a mean age of 68 (range 21–96) years. Upper GIB accounted for 31 (37%) of the cases. All patients with UGIB had an initial diagnostic esophagogastroduodenoscopy. Initial management consisted of therapeutic endoscopic intervention once the cause of bleeding was identified. A second endoscopy was performed in 15 of 24 (63%) patients with confirmed gastric or duodenal ulcer as a cause for UGIB. Of the 52 patients with LGIB, only 35 (67%) underwent complete colonoscopy before angiography. Patient characteristics are summarized in Table 1.

Active contrast medium extravasation on initial angiography was present for 18 of 83 (22%) patients. Of these, embolization was technically successful in 15 (83%) patients with 3 technical failures. In all 3 cases, the cause for technical failure was inability to catheterize the target vessel owing to severe atherosclerosis. These 3 patients all required operative intervention to control the identified bleeding. Only 2 patients who initially did not demonstrate active contrast medium extravasation underwent heparin challenge: 1 patient had a positive angiogram whereas the other did not. Of the 65 patients who had a negative initial angiogram, 10 (15%) underwent blind embolization. Overall, embolization was performed in 25 of 83 (30%) patients

Characteristic	No.	(%)*
Age, mean yr	67.	.8
Sex		
Male	56	(67)
Female	27	(32)
Cardiac comorbidity	48	(58)
Anticoagulant use	45	(54)
UGIB	31	(37)
Gastric or duodenal ulcer	24	(77)
Angiodysplasia	3	(10)
Malignancy	2	(6)
Other	2	(6)
LGIB	52	(63)
Diverticulosis	30	(58)
Malignancy	7	(13)
Localized to small bowel	5	(10)
Hemorrhoids	4	(8)
Other	7	(13)

who underwent initial mesenteric angiographies. The mean length of stay in hospital was 23 (range 1–163) days. Overall 30-day mortality was 16%.

Active contrast medium extravasation on initial angiography was associated with a systolic blood pressure of less than 90 mm Hg with or without concurrent pharmacologic hemodynamic support as well as a greater need for packed red blood cell (PRBC) and fresh frozen plasma transfusions in the 24 hours preprocedure. Anticoagulant use and the need for platelet transfusions were not associated with a positive angiogram. A UGIB was more likely to demonstrate active contrast extravasation than an LGIB. These results are summarized in Table 2. On multivariate analysis, each unit of PRBC transfused in the 24 hours preangiography increased the risk of a positive angiogram by 30% (hazard ratio [HR] 1.3, 95% confidence interval [CI] 1.2–1.6).

Overall, patients who underwent embolization did not experience a significant reduction in the incidence of recurrent bleeding, surgical intervention or length of stay in hospital compared with those who did not undergo embolization (Table 3). However, 30-day mortality was significantly greater in the embolization than the nonembolization group (33% v. 7%, p = 0.006), and these patients were more likely to have a hemodynamic compromise as a direct result of the GIB (73% v. 28%, p = 0.001), which may explain the greater mortality. Patients undergoing blind embolization were excluded and analyzed separately because they were high-risk surgical candidates owing to their medical comorbidities and represented an important selection bias.

We compared patients undergoing angioembolization in the presence of active contrast medium extravasation with patients undergoing blind embolization. We found no differences in age (63.5 v. 65.6 yr, p = 0.77), sex (73% v.

Table 2. Comparison of active versus no active contrast medium extravasation				
Characteristic	Active extravasation, $n = 18$	No active extravasation, $n = 65$	p value	
Age, mean (range) yr	72 (21–96)	69 (36–95)	0.61	
Male sex, %	67	66	> 0.99	
Location of GIB, %			0.17	
Upper	50	29		
Lower	50	60		
Presence of coagulopathy, %	57	44	0.43	
Tumour bleed, %	28	23	0.76	
SBP < 90 mm Hg ± vasopressor use at time of procedure, %	67	28	0.005	
Transfusions 24 h preprocedure, mean (range) no. units				
Packed red blood cells	5.3 (1–9)	2.8 (0-9)	< 0.001	
Fresh frozen plasma	4.8 (0-12)	1.7 (0-16)	0.002	
Platelets	2.9 (0–18)	2.1 (0-15)	0.42	
GIB = gastrointestinal bleeding; SBP =	systolic blood pres	sure.		

70% male, p = 0.86), UGIB (73% v. 80%, p = 0.10), coagulopathy (47% v. 70%, p = 0.25) or tumour bleed (7% v. 10%, p = 0.91) between the 2 groups. Patients in the active extravasation group were more likely than those in the blind embolization group to be hemodynamically compromised (73% v. 30%, p = 0.029), in keeping with the previous results. There were also no differences between these 2 groups in recurrent bleeding (53% v. 40%, p = 0.51), surgical intervention (13% v. 10%, p = 0.80), length of stay in hospital (28.1 v. 34.2 d, p = 0.67) or 30-day mortality (33%) v. 40%, p = 0.73). All patients who underwent blind embolization had a bleeding source identified via endoscopy and thus underwent nonselective angioembolization based on endoscopic localization. Table 4 reports the bleeding etiology and embolized vessels for each patient who underwent blind embolization. All of the patients who died were critically ill and were already admitted to the intensive care unit (ICU) for severe sepsis (n = 1), graft versus host disease (n = 1), complications of systemic lupus erythematosus (n = 1) and severe cardiogenic shock (n = 1) when the GIB occurred.

Among patients without active contrast medium extravasation, there were no differences between the embolization and nonembolization groups in sex (70% v. 66% male, p = 0.78), age (65.7 v. 69.3 yr, p = 0.41), cardiac comorbidities (60% v. 36%, p = 0.18) or hemodynamic instability (30% v. 27%, p = 0.86). More patients in the blind embolization group than the nonembolization group had UGIB (80% v. 26%, p = 0.001). Blind embolization was also associated with a longer length of stay in the ICU (17.1 v. 9.0 d, p = 0.05) and 30-day mortality (40% v. 7.3%,p = 0.004) than nonembolization; however, we found no difference in recurrent bleeding (40% v. 51%, p = 0.53) or surgical intervention (10 v. 24%, p = 0.34). On multivariate Cox proportional hazards analysis, blind embolization was found to be an independent predictor for 30-day mortality (HR 9.2, 95% CI 1.5–55.9).

There were 11 complications in total: 3 technical failures owing to the inability to embolize despite active extravasation, 4 minor complications not resulting in significant morbidity or mortality and 4 major complications resulting in significant morbidity or mortality (Table 5).

DISCUSSION

Despite advances in endoscopic techniques, surgical interventions, critical care and pharmacotherapy, acute GIB remains a common and potentially life-threatening event that requires prompt diagnosis and definitive treatment.

Angioembolization has been shown to be effective and relatively safe in the treatment of acute UGIB and LGIB. 19-21 However, it requires specialized equipment and experienced interventional radiologists, preventing its widespread access beyond large centres. It has been shown, albeit in retrospective studies only, to be at least as equally effective as surgery after endoscopic failure for acute UGIB. Ripoll and colleagues²² found no differences in recurrent bleeding, need for additional surgery or mortality despite the embolization group having more comorbid conditions. Eriksson and colleagues²³ also found that 30-day mortality was significantly lower in patients treated with angioembolization than those treated with surgery, even though they were on average older and had more comorbidities. To our knowledge, no published randomized trials exist to demonstrate the superiority of one method over the other. There are no studies comparing arterial embolization to surgery for acute LGIB; however, the role of angiography in this setting is still unclear.

In the present study, only 22% of mesenteric angiographies performed for acute GIB demonstrated active contrast medium extravasation. We identified hemodynamic instability and blood product transfusion requirement as predictors for active contrast extravasation. On multivariate analysis, each unit of PRBCs increased the likelihood of

	Group, no. (%)*				
Characteristic	Embolization with active extravasation, $n = 15$		No embolization, $n = 58$		<i>p</i> value
Age, mean (range) yr	64	(21–96)	69	(36–95)	0.16
Male sex	11	(73)	37	(64)	0.47
UGIB	7	(47)	16	(28)	0.16
Presence of coagulopathy	7	(47)	31	(53)	0.64
Tumour bleed	1	(7)	5	(9)	0.81
Hemodynamic instability at time of procedure	11	(73)	16	(28)	0.001
Recurrent bleeding	8	(53)	30	(52)	0.91
Surgical intervention	2	(13)	15	(26)	0.31
ICU length of stay, mean (range) d	10.5	(1–32)	9.4	(0-62)	0.79
Overall length of stay, mean (range) d	28.1	(2–161)	27.5	(1–163)	0.95
30-day mortality	5	(33)	4	(7)	0.006

active contrast extravasation by 30%. Intuitively, these results demonstrate that patients who have evidence of active bleeding are more likely to have a positive angiogram. A similar study by Kim and colleagues²⁴ reporting a positive angiogram rate of 50% identified hemodynamic stability and a lower GI source as predictors for a negative angiogram. In the present study, a lower GI source was also more likely to result in a negative angiogram, although this finding was not statistically significant. The intermittent nature of even massive acute GIBs and the variable bleeding rates can limit the ability of angiography to demonstrate active extravasation, especially in acute LGIB.25 Several other studies have attempted to identify predictors for a positive angiogram. Abbas and colleagues26 reported hemodynamic instability, a drop in hemoglobin and PRBC transfusions as predictors of active extravasation in acute LGIB. Conversely, Pennoyer and colleagues²⁷ did not identify any significant predictors. This discrepancy in results may be an illustration of the heterogeneity of the population with GIB, making the generalizability of study results very difficult.²⁸

Almost all of the more recent series have reported a technical success rate of angioembolization of greater than 95%, 12,29,30 although the failure rate may be as high as 50%. Repeat angiography may be equally effective. In the present study, technical success occurred in 25 of 28 (89%) attempted embolizations. Clinically significant recurrent bleeding requiring additional interventions occurred in 12 of 25 (48%) patients after embolization. The high rate of rebleed after embolization was greater than expected. One hypothesis is that the extensive collateral circulation of the stomach may limit the degree of hemostasis from embolization of a single artery. In the present study, we were not able to identify any predictors for angiographic failure.

Embolization can also be performed in the absence of active extravasation (i.e., blind embolization). In a comparison between embolization with a positive angiogram versus

Table 4. Demographic and clinical characteristics of patients who underwent blind embolization					
Patient	Sex	Age, yr	Etiology	Embolized artery	
1	М	69	Duodenal ulcer	Gastroduodenal artery	
2	M	88	Rectal cancer	Hemorrhoidal artery	
3	M	69	Duodenal ulcer	Gastroduodenal artery	
4	M	57	Gastric ulcer	Left gastric artery	
5	М	63	Small bowel angiodysplasia	Jejunal artery branch	
6	F	82	Gastric hematoma	Gastroduodenal artery	
7	M	55	Gastric ulcer	Left gastric artery	
8	М	76	Duodenal ulcer	Gastroduodenal artery, right gastroepiploic artery	
9	F	60	Duodenal ulcer	Gastroduodenal artery	
10	F	38	Rectal ulcer	Bilateral anterior division of internal iliac artery	
F = female	e; M = n	nale.			

blind embolization, Padia and colleagues³³ demonstrated no difference in blood product transfusions postprocedure, subsequent surgical intervention or 30-day mortality. Our data show similar outcomes. However, among patients without active contrast extravasation, our results demonstrate that blind embolization was associated with a longer stay in the ICU and increased 30-day mortality when compared with patients who were not embolized. As mentioned previously, a large proportion of patients undergoing blind embolization were already critically ill before the onset of massive GIB. It is highly likely that the physiologic status of these patients contributed to the high morbidity and mortality in the blind embolization group. The effectiveness of blind embolization for UGIB remains questionable for the same reasons as for embolization in the presence of active contrast extravasation. No studies exist describing the effectiveness of blind embolization in acute LGIB, as accurate localization of the bleed is required to perform angioembolization. In this setting, identifying accurate predictors for active contrast extravasation can help guide what intervention would be most appropriate in the patient with severe LGIB. However, if the source of LGIB is identified and uncontrolled with endoscopic therapy, then angioembolization may have some role in subsequent management. Two of the 10 patients who underwent blind embolization had an identified source of LGIB (Table 5). Neither patient had recurrent bleeding.

Eight patients in our series experienced either minor or major complications. Four patients had minor complications as a direct result of mesenteric angiography. A femoral hematoma at the puncture site occurred in 3 patients, and in 1 patient the embolization coil migrated into another artery. None of these 4 patients had clinically important morbidity as a result of these minor complications; 4 other patients experienced major complications. Large bowel ischemia requiring surgical intervention occurred in 1 patient, and another had massive hematemesis and blood per ileostomy following heparin challenge, requiring substantial blood product transfusion and endotracheal

Table 5. Complications of patients who underwent embolization	
Complication	No.
Technical failure	
Unable to identify exact bleeding vessel	1
Unable to catheterize bleeding vessel	2
Minor complications	
Femoral hematoma	3
Migration of coil	1
Major complications	
Duodenal necrosis	1
Gastresophageal junction perforation	1
Large bowel ischemia	1
Massive hematemesis following heparin challenge	1
Total	11

intubation. These 2 major complications were directly attributed to the mesenteric angiography. The etiologies of the other 2 major complications were not clear. Duodenal necrosis occurred in the 1 patient and gastroesophageal junction perforation occurred in the other. Embolization was performed in both of these patients and was preceded by multiple attempts of endoscopic epinephrine injections before angiography and embolization. It is unclear whether these complications occurred as a result of endoscopic therapy or angiographic embolization.

Limitations

The principal shortcoming of this study is its retrospective design. A selection bias may exist, as angiography and embolization are more often performed in patients who are poor surgical candidates. Additionally, we did not compare outcomes between surgical intervention and angiography. Another important limitation of this study is the inclusion of both UGIB and LGIB in the analysis. The use of angiography in the decision-making algorithm may differ for acute UGIB and LGIB. Patients with massive UGIB all undergo initial endoscopy for localization and therapeutic attempt before angiography. However, urgent colonoscopy for massive LGIB is technically more difficult with less potential therapeutic benefit, especially in patients with massive diverticular bleeding. Clinical outcomes may have been impacted by these confounders. Despite these limitations, this study remains valuable in looking at predictors of active contrast medium extravasation and characterizing the outcomes of angiography, as few studies to date have reported on the outcomes of negative angiograms.

CONCLUSION

Active contrast medium extravasation on mesenteric angiography for acute GIB can be predicted by hemodynamic instability and significant blood product transfusion requirements. Each unit of PRBCs transfused within a 24-hour period increases the likelihood of a positive angiogram by 30%. Technical success was 83% in our series. Angioembolization was associated with high 30-day mortality. It is unclear whether the high morbidity and mortality are due to the procedure itself or to the physiologic status of the patients. In patients without active contrast medium extravasation, blind embolization was associated with significantly higher 30-day mortality, although it is unclear whether it was a result of the procedure itself or if it was a marker of critical illness. Major complications of mesenteric angiography were uncommon. There is a need for large, prospective randomized trials to definitively characterize the indications and outcomes of mesenteric angiography and angioembolization in the management of acute GIB.

Competing interests: None declared.

Contributors: L. Lee, P. Fata and T. Razek designed the study. L. Lee and S. Najmeh acquired the data, which L. Lee, S. Iqbal, P. Fata, T. Razek and K. Khwaja analyzed. L. Lee, S. Najmeh, S. Iqbal, P. Fata and K. Khwaja wrote the article, which L. Lee, S. Iqbal, T. Razek and K. Khwaja reviewed. All authors approved its publication.

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RECHERCHE

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