International Journal of Gastrointestinal Intervention

journal homepage: www.ijgii.org

Review Article

Endovascular hemostasis for endoscopic procedure-related gastrointestinal bleeding

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ABSTRACT

Gastrointestinal (GI) bleeding is a common complication of various endoscopic procedures. In most cases, GI bleeding responds to conservative management. And if indicated, endoscopic hemostasis is performed. However, if endoscopic hemostasis fails due to massive bleeding or hemodynamically unstable patients, alternative treatment options, such as endovascular hemostasis or surgery, should be considered. As endoscopic procedures have become more diverse, there have been reports of interventional treatment of endoscopic, procedure-related GI bleeding. In this article we will discuss the endovascular diagnosis and treatment of endoscopic, procedure-related GI bleeding.

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Keywords: Angiography; Embolization, therapeutic; Endoscopy; Gastrointestinal hemorrhage

Introduction

Gastrointestinal (GI) bleeding occurs due to various causes including peptic ulcer disease, benign and malignant tumors, and even an iatrogenic cause.¹ If not treated properly, life-threatening hemorrhage can occur. Various endoscopic procedures can cause GI bleeding. If GI bleeding does not respond to medical treatment, endoscopic hemostasis is a first choice for treatment of GI bleeding.^{2,3} Endoscopic procedures can identify the bleeding site and then directly perform hemostasis. However, endoscopic procedures may fail due to massive bleeding or hemodynamically unstable patients. Approximately 10% to 30% of endoscopically treated patients have repeated GI bleeding.⁴ In patients with endoscopic hemostasis failure or in technically infeasible patients, emergency surgery and endovascular hemostasis are alternative treatment options.^{3,5}

Since Nusbaum et al⁶ has reported transarterial infusion for variceal bleeding in 1968, endovascular hemostasis for GI bleeding has been developed.^{6,7} In addition, improvement of microcatheter and embolic materials increased the role of endovascular hemostasis in patients with lower GI bleeding.⁸ Endovascular hemostasis is a better option than surgery in cases where the location of bleeding is uncertain or the patient's vitality is unstable.¹

Also, another advantage of endovascular hemostasis is that it can reduce the patient morbidity and mortality secondary to surgery.^{4,9} There are many published reports regarding endovascular hemostasis in GI bleeding due to various causes.^{5,10} In this article we will discuss the endovascular hemostasis of endoscopic procedure-related GI bleeding.

Indications and Contraindications of Endovascular Hemostasis

The typical candidates for endovascular hemostasis include the following: 1) those with acute GI bleeding that is refractory to endoscopic hemostasis; 2) those with massive bleeding that requires transfusion of more than four units of blood over 24 hours or those with unstable hemodynamic status, i.e., systolic blood pressure < 100 mmHg and heart rate > 100 beats per minute; and 3) those with recurrent bleeding.^{5,10}

Relative contraindications include renal insufficiency and uncorrectable coagulopathy. For patients with adverse reactions to iodine contrast medium, alternative contrast media, such as carbon dioxide, should be used.

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Received June 18, 2019; Revised July 18, 2019; Accepted July 18, 2019

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Imaging Modality for GI Bleeding

Endoscopy is the first choice for the diagnosis and treatment of overt GI bleeding. However, if endoscopy is not available due to hemodynamic instability or massive bleeding, other diagnostic tools are required.

Radionuclide technetium-99m-tagged red blood cell scan (Tc99m RBC scan) is the most sensitive imaging modality for overt GI bleeding. It is a non-invasive modality and can detect GI bleeding from the amounts of approximately 0.1 mL/min as well as intermittent and venous bleeding.^{9,11} However, it cannot precisely detect the anatomic source of the bleeding. In addition, its long scan time makes it unsuitable for emergency patients.

Computed tomography angiography (CTA) scanning is able to detect bleeding from the amounts of approximately 0.3 mL/min.^{12,13} CTA has the advantages of greater availability, speed, and non-invasiveness. CTA scanning shows a possible cause of bleeding and surrounding anatomic structures. Also, CTA scanning can show the complete vascular anatomy and thus allow better planning of subsequent endovascular hemostasis.⁹

Conventional digital subtraction angiography (DSA) can identify the entire mesenteric systems, thus allowing the identification of rarer sites of hemorrhage, such as hemobilia and hemosuccus pancreaticus.^{1,14,15} DSA is able to detect bleeding from amounts of approximately 0.5 mL/min.⁹ Its sensitivity remains at about 60%, but its specificity approaches 100%.¹ The major limitation of angiography is related to the intermittent nature of bleeding which can result in a negative result if the bleeding has temporarily stopped at the time of contrast injection.

Angiographic Findings of Active Bleeding

The direct angiographic findings of bleeding are visualization of active contrast extravasation and contrast pooling in the venous phase. However, these findings cannot be confirmed in all cases of active bleeding. In one study about non-variceal upper GI bleeding, active contrast extravasation was only seen in 54% of the cases.¹⁶

Indirect angiographic findings are vessel cutoff/spasm, aneurysms/pseudoaneurysms, pseudovein sign, arteriovenous/arterioportal shunting, and neovascularity. The pseudovein sign refers to extravasated contrast media pooling within the gastric rugae or mucosal bowel folds, and thus mimicking a vein. The pseudovein sign can be distinguished from the true vein by persistence beyond the venous phase of contrast injection.

Techniques of Endovascular Hemostasis

Endovascular hemostasis for GI bleeding requires an accurate and complete understanding of the vascular anatomy. The GI tract has a complex network of anastomotic arteries providing a rich blood supply.¹ It decreases the incidence of severe complications, including severe ischemia or embolization of unwanted organs. However, due to this anastomotic blood supply, effective endovascular hemostasis may not be able to be performed. In particular, when bleeding occurs in an area with a dual blood supply, such as the splenic flexure of the colon (middle and left colic arteries), the duodenum (superior and inferior pancreaticoduodenal arteries), lesser curvature of the stomach (right and left gastric arteries), great curvature of the stomach (right and left gastroepiploic arteries), and the distal rectum (superior and inferior hemorrhoidal arteries), hemostasis is achieved by embolization of the proximal and distal limbs of the vascular arcade.^{5,17} Angiography

to confirm the effective hemostasis should also be performed in both limbs of the vascular arcade.^{5,17} As a premedication, Glucagon and scopolamine butylbromide are useful for decreased bowel motility and motion artifact during the procedure.¹⁸

Provocative angiography using tolazoline (usually 15–30 mg) can improve the sensitivity for diagnosing GI bleeding.^{9,18} Also, longer injection durations or use of carbon dioxide for contrast medium can improve the detection of small bleeding.¹⁶ Endoscopic clips placed around the area of bleeding during pre-embolization endoscopy can help to accurately localize the bleeding vessels. It can therefore increase the success rate and reduce the time of endovascular hemostasis.¹⁹ If no extravasation is seen, despite the injection of contrast medium, the branches terminating at the clip are then superselected using microcatheter techniques and are embolized.^{20,21} Oblique views can provide a clearer view of colic vessels in flexures. In addition, right and left anterior oblique views open up hepatic and splenic flexures. The major complications after endovascular hemostasis are bowel ischemia and infarction, and with rates varying from 0.04% to 9%.²² Accurate and careful selection of the bleeding focus and gentle injection of embolic materials are important in order to reduce major complications after endovascular hemostasis.

Embolic Materials

The choice of the embolic agent depends on a combination of the vascular anatomy, angiographic findings, the achievable catheter position, and the operator's preference. The most common embolic agents are metallic coils and gelatin sponge particles (GSPs).⁵ Metallic coils are permanent, embolic materials made with stainless steel or platinum. They cause mechanical occlusion, platelet activation, and clotting cascade.⁵ However, the use of coils as the only embolic agent is associated with a higher risk of early bleeding recurrence compared with adding polyvinyl alcohol or GSPs to coils.^{4,23} GSP is a temporary embolic material. It causes mechanical occlusion and structural support to the thrombus. Most vessels recanalize in a few weeks to a few months.

N-butyl cyanoacrylate (NBCA), also called glue, is a liquid permanent embolic material.⁵ It is difficult to control due to its nonradiopaque nature and rapid polymerization with blood. Therefore, lipiodol is used as a diluting agent to slow the polymerization reaction and provide radiopacity for the solution.²⁴ NBCA should be used as a mixture with lipiodol under fluoroscopic guidance. Usually, the NBCA:lipiodol ratio ranges from 1:1 to 1:4. It is advantageous for massive bleeding that requires urgent hemostasis, especially in patients with coagulopathy.²⁵ Before NBCA injection, flushing the catheter with 5% dextrose solution is important to prevent rapid polymerization within the catheter.

Endoscopic Procedure-Related GI Bleeding

Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD)

EMR and ESD are effective and minimally invasive procedures for upper GI epithelial and subepithelial lesions. They are useful techniques for treating early gastric cancer without lymph node metastasis, other polyps, and submucosal lesions. Bleeding is the most common complication of endoscopic procedures. It can be classified into immediate (intra-procedural) or delayed (post-procedural) bleeding.^{26,27} Immediate bleeding during ESD and EMR procedures is common, with reported rates varying from 22.6% to 90.6%.²⁸ Endoscopic hemostasis is performed by using

contact coagulation or hemostatic forceps. Most intra-procedural bleeding resolves without further intervention. Post-procedure bleeding occurs within 24 hours of ESD, but it can occur also two weeks after ESD.^{2,29} The incidence of bleeding after gastric ESD has been reported to range from 1.8% to 15.6%.^{29,30} Bleeding rates after esophageal or colorectal ESD are relatively lower than those of gastric ESD. Reported risk factors that increase post-ESD bleeding are dual antiplatelet therapy and heparin bridge therapy. Also, large resection size (> 40 mm) is a risk factor for post-ESD bleeding.²⁹ Other known risk factors for post-ESD bleeding in gastric epithelial neoplasms is dialysis, long operation time (≥ 75 min), and poor control of bleeding during ESD.³¹

The role of endovascular hemostasis in procedure-related bleeding is as important as that in an endoscopic procedure or emergent surgery (Fig. 1). However, information regarding the role of endovascular hemostasis has rarely been published. In one report regarding ESD for gastric neoplasm, post-ESD bleeding occurred in 94 patients out of 1,591. Among them, three angiographic embolization procedures were performed.³² Komatsu et al² performed transcatheter arterial embolization with a microcoil and GSP through the right gastric artery when there was immediate bleeding during gastric ESD. Lee et al³³ used microcoils for post-ESD bleeding from the side branch of the left gastric artery. Park et al³⁴ reported one case of gastric intramural hematoma caused by EMR that required hemoclipping and transcatheter arterial embolization in the left gastric artery.

There are no preferable embolic materials which could be used for management of the bleeding. However, there are cases in which there is no apparent angiographic finding of active bleeding. In this case, there are several reports recommending empirical embolization of the left gastric or gastroduodenal artery depending on the location of the bleeding focus.^{22,35,36} The left gastric artery constitutes 85% of all of the angiographically documented upper GB bleeding sites.³⁵ In general, embolization of the left gastric artery does not cause clinically serious complications. Laursen et al³⁷ reported that supplementary transcatheter arterial embolization is potentially useful in patients with high-risk peptic ulcer bleeding and it can reduce the rate of rebleeding and the length of a patient's hospital stay. There are a few reports regarding empirical embolization in procedure-related GI bleeding. Park et al³⁴ performed prophylactic transcatheter arterial embolization after embolization in a patient with gastric EMR-induced GI bleeding.

Endoscopic ultrasound (EUS)-guided procedures

EUS has been a diagnostic procedure concentrating on structural identification and staging of GI cancers. Also, because EUS

allows real-time visualization of structures beyond the endoscopic view, it has been used for various therapeutic interventions (EUS-guided interventions in special situations). EUS-guided drainage is an effective technique for use with patients with failed endoscopic retrograde cholangiopancreatography (ERCP) and/or altered surgical anatomy.

Peripancreatic fluid collection or walled-off necrosis is a common complication of pancreatitis. Asymptomatic fluid collection of walled-off necrosis can be managed conservatively. Indications for drainage are intractable pain, increase in size, infection, and gastric outlet or biliary obstruction.³⁸ EUS-guided pancreatic drainage is effective with a lower morbidity compared to the other platforms.³⁹ However, it requires the highest technical skill because of the difficulty of EUS-guided puncture and the calcified pancreatic tissue.⁴⁰ The complications of these procedures are bleeding, bowel perforation, acute pancreatitis, and infection. The complications of EUS-guided cystogastrostomy occur at a rate of 17% to 19% in the patients.⁴¹ Among the various complications, bleeding has been reported as 5% to 15%.³⁸ There are some reports on endovascular hemostasis in bleeding after EUS-guided pancreatic drainage (Fig. 2). Brandon et al³⁸ performed coil embolization of pseudoaneurysm in both the right and left gastric arteries after EUS-guided cystogastrostomy for a pancreatic pseudocyst. Kurihara et al⁴² reported a case of a post-procedure complication of EUS-guided pancreatic drainage. After use of the EUS-guided rendezvous technique, a pancreatic pseudocyst with splenic artery aneurysm developed in this patient with pancreatic head cancer, although he recovered with the use of selective angiography and embolization.

The choice of EUS-guided biliary drainage depends on the inherent reason for failed conventional ERCP, patient anatomy, indication for biliary drainage, and operator preference.⁴³ In a recent meta-analysis, the bleeding risk associated with EUS-guided biliary drainage is 4.03%.⁴⁴ Most bleeding complications can initially be treated conservatively, however, additional procedures such as embolization can be necessary for hemostasis (Fig. 3). Prachayakul et al⁴⁵ reported a case of coil embolization of a left hepatic artery pseudoaneurysm after EUS-guided hepaticogastrostomy for biliary drainage. The cause of bleeding was presumed to be the creation of the hepaticogastrostomy tract using a stent retriever.

Percutaneous endoscopic gastrostomy (PEG)

Indications for gastrostomy tube use are for nutrition support in patients with an impaired swallowing mechanism associated with neurological and neoplastic conditions.^{46,47} Gastrostomy tube insertion is performed surgically or percutaneous under endo-

Fig. 1. Active bleeding after endoscopic mucosal resection (EMR) for gastric polyp. (A) EMR for a gastric polyp is performed. (B) Endoscopy image 10 days after EMR shows active bleeding on the EMR sites. Endoscopic hemostasis was unsuccessful. (C) Left gastric arteriogram shows active bleeding from the branch of the left gastric artery (arrow), matched with the endoscopic hemostasis site. (D) Embolization using N-butyl cyanoacrylate was performed without any complications.

Fig. 2. Active bleeding after endoscopic ultrasound (EUS)-guided pancreatic drainage. (A) Abdominal computed tomography (CT) scan shows a peripancreatic fluid collection between the stomach and the spleen. (B) Brownish turbid fluid was drained through an EUS-guided, inserted cystogastrostomy stent. (C) Three days after the procedure, an abdominal CT scan showed high attenuation of the hematoma within the stomach but without an active bleeding focus. (D) Splenic arteriogram shows a pseudoaneurysm-like appearance (arrows) without its short gastric artery continuation into the spleen. (E) Selective angiogram with the microcatheter tip at the location of the pseudoaneurysm-like appearance, shows active bleeding into the pseudoaneurysm sac. N-butyl cyanoacrylate embolization was performed (not shown). (F) Post-embolization splenic arteriogram shows no further visualization of the pseudoaneurysm-like appearance. Clinically, the bleeding was thereby controlled.

Fig. 3. Active bleeding after endoscopic ultrasound (EUS)-guided, biliary drainage for ampulla of the Vater cancer patient. (A) Endoscopic image shows a hepaticogastrostomy stent which was inserted under the EUS in the stomach. (B) Non-enhanced abdominal computed tomography scan shows a hepaticogastrostomy stent with a hematoma within the stent and common hepatic duct (arrows). There was no active contrast extravasation. Endoscopy was not possible due to the large amount of gastric contents. (C) Left hepatic arteriogram shows a large pseudoaneurysm (arrow) around the hepaticogastrostomy stent insertion site. (D) Embolization using a coil and N-butyl cyanoacrylate was performed (not shown). The post-embolization celiac angiogram shows no more active bleeding.

scopic or fluoroscopic guidance. PEG is one of the most common endoscopic procedure worldwide. It is usually considered to be a safe procedure, but there may be several major complications. Reported bleeding rates after PEG insertion vary from 0% to 2.5%.⁴⁸ Major causes are esophagitis, gastric pressure ulcers, concomitant peptic ulcer disease, and vessel injury is rare.⁴⁹ Bleeding from the PEG tract, gastric artery, splenic or mesenteric vein injuries have been also reported.⁴⁶ Endoscopy is superior for localizing the bleeding site, characterizing the cause of bleeding, and showing the relationship between the bleeding site and the gastrostomy tube.⁵⁰ However, endoscopy may be limited by several factors including the presence of comorbid illnesses, active bleeding, bleeding vessels larger than 2 mm, and endoscopic blind spots, all of which may increase hemostatic failure for upper GI bleeding.⁵⁰ In these situations, endovascular embolization can be used effectively (Fig. 4).

There have been a few reports regarding endovascular embolization for bleeding after PEG. Lewis et al⁵¹ reported a case of endovascular embolization for bleeding from both the right and left gastropiploic arteries after PEG insertion. Lee et al⁵² reported a case of bleeding from the pancreatic branch of the superior

mesenteric artery after PEG insertion. It was identified on abdominal computed tomography (CT); however, as angiography had revealed no active bleeding, embolization using gelfoam was performed based on the abdominal CT findings. Hong et al⁵³ reported a case of a ruptured left gastric artery pseudoaneurysm complicating PEG insertion. Embolization using histoacryl was performed without any complications.

Endoscopic ampullectomy

Tumors of the ampulla of Vater are rare. Among the various tumors arising from the ampulla, adenomas are most frequently encountered. Ampullary adenomas occur sporadically or are associated with hereditary polyposis syndromes, including familial adenomatous polyposis and its variants. Ampullary adenomas may follow an adenoma-to-carcinoma sequence. Therefore, ampullary adenomas are considered as a precancerous lesion and removal is required.⁵⁴ Since endoscopic ampullectomy was first described in 1983, it has been used as a replacement for surgical treatment of ampullary adenoma in selected patients.^{55,56} Endoscopic ampullectomy has lower morbidity and mortality rates than surgical ap-

Fig. 4. Active bleeding after percutaneous endoscopic gastrostomy (PEG). (A) Endoscopy shows a PEG tube. (B) Non-enhanced abdominal computed tomography scan shows a large hematoma collection in the omentum, mesentery, and perisplenic spaces (arrows). (C) Splenic arteriogram showed vessel cut-off of the prominent left gastroepiploic artery (arrowhead). (D) Coil embolization was performed without any complications.

Fig. 5. Active bleeding after endoscopic ampullectomy for ampullary adenoma. (A) The initial endoscopic ultrasound showed an approximately 0.9-cm sized, round, and low echoic mass on the ampulla of Vater. (B) Profuse bleeding was noted on endoscopy. Endoscopic bleeding control was unsuccessful. (C) A celiac angiogram shows contrast extravasation (arrow) from the inferior pancreaticoduodenal artery. (D) After embolization using N-butyl cyanoacrylate, the celiac angiogram showed no further bleeding focus.

proaches. Endoscopic ampullectomy can be performed in patients with smaller lesions, i.e., less than 3 cm in size, that do not contain carcinoma and in inoperable patients.⁵⁶

Complications of endoscopic ampullectomy are pancreatitis (0%–25%), bleeding (0%–25%), perforation (0%–4%), cholangitis (0%–2%), and papillary stenosis (0%–8%).⁵⁶ Most bleeding after endoscopic ampullectomy can be controlled by conservative treatment and endoscopic hemostasis. If massive bleeding occurs, emergent embolization is initially preferred to surgery (Fig. 5). There were a few published manuscripts regarding endovascular hemostasis of bleeding after endoscopic ampullectomy. In one single center study with 91 patients, 11 patients had bleeding after endoscopic ampullectomy. Among them, four patients were managed with endoscopic hemostasis and one patient required transcatheter arterial embolization.⁵⁷ In another retrospective cohort study with 110 patients, 11 patients had post-procedural bleeding. In one patient, bleeding was managed by coil embolization of the gastroduodenal artery.⁵⁸

Conclusion

Endoscopic, procedure-related bleeding is an important adverse effect for which immediate treatment is required. Usually, conservative management and endoscopic hemostasis are effective for procedure-related GI bleeding, but other treatment options may be necessary in some patients. Endovascular hemostasis is a

safe and effective treatment for endoscopic, procedure-related GI bleeding. It is required when endoscopic therapy is not feasible or has failed.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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