Review Article

Endovascular treatment of pancreatitis-related gastrointestinal bleeding

Seung Yeon Noh, Ji Hoon Shin*

A B S T R A C T

Hemorrhage following pancreatitis may become complicated during the disease course and with possibly fatal consequences. Radiologic findings are as follows: the presence of hematomas, hemorrhagic pseudocysts, extravasation of contrast media or the formation of arterial pseudoaneurysms. The digital subtraction angiography findings are as follows: contrast extravasation due to arterial rupture; pseudoaneurysm formation; and luminal irregularity. A pseudoaneurysm is considered to be treated as soon as detected due to its risk of rupture. Endovascular management, which includes embolization using coils, N-butyl cyanoacrylate, gelatin sponge, stents, and thrombin, is an effective option for the treatment for pancreatitis-related bleeding.

Introduction

The incidence of bleeding complications following pancreatitis varies between 1.2% and 14.5% in patients with acute and exacerbated chronic pancreatitis. These conditions can occasionally be potentially fatal when remaining untreated and causing the overall mortality rate to reach 52.4%.1–3 Traditionally, the major treatment option for such a condition has been known to be surgery, i.e., ligation or repair of the bleeding vessel followed by external drainage of the pseudocyst, Roux-en-Y cystojejunostomy or distal pancreatectomy; however, currently there have been an increase in numbers of endovascular management for treating bleeding complications in pancreatitis patients. Endovascular treatment is known to be superior or comparable to surgical management, especially in patients with systemic comorbidities and for whom it is difficult to undergo general anesthesia, as well as in patients in whom surgery is considered to be difficult due to adjacent inflammatory and adhesive changes around the pancreas.5-8 One previously published report suggested that embolization therapy was associated with lower transfusion requirements and a shorter hospital stay compared with those of surgery.5 Furthermore, one previous report demonstrated that there were more frequent bleeding complications in patients with early surgical treatment, and which is probably due to iatrogenic vascular injury when using techniques such as gauze packing or drainage tube insertion.2,6

In this review, we deal with pancreatitis-related gastrointestinal (GI) bleeding, while focusing on the endovascular treatment.

Pathogenesis and Demographic Findings

The severity of acute pancreatitis is responsible for the bleeding risk, i.e., 1.5% in interstitial pancreatitis versus 13.5% in acute necrotizing pancreatitis.7 Sepsis, fluid collection, organ failure, and the number of previous surgeries were found to be additional risk factors for hemorrhage.3,7 However, the etiology of acute pancreatitis does not seem to have any prognostic meaning and bleeding in patients with alcoholic, biliary or idiopathic pancreatitis was associated with similar mortality rates.1 Flati et al1 suggested four types of pathogenesis of bleeding in pancreatitis, especially in acute pancreatitis. (a) Local severe inflammation and necrosis cause the local spread of the necrotizing process and extravasation of exocrine proteolytic/lipolytic enzyme-rich fluids, thus causing damage of the adjacent vascular...
structure and rendering the vessels susceptible to rupture or pseudaneurysm formation. (b) Abscess, enzymatic action, bacterial action, and abscess drainage procedures together may cause GI perforations, vessel wall weakening, and disruption with hemorrhage. (c) Pseudocysts may exert compression, ischemic changes, and elastolytic damage of vessel walls and leading to acute rupture or pseudaneurysm formation with eventual spontaneous disruption and massive hemorrhage. (d) Local sequelae of pancreatitis may cause splenic vein thrombosis resulting in left-sided portal hypertension and gastroesophageal bleeding from a variceal rupture. According to a previously published report, the risk factors for high mortality rates, are as follows: venous bleeding; bleeding via external drainage after necrosectomy; and a complication of necrosis, mortality rates of 50%, 100%, and 39.3%, respectively.

Clinical and Radiologic/Angiographic Findings

Clinical manifestation of bleeding in pancreatitis patients varies from sudden onset or exacerbation of pre-existing abdominal pain, abdominal distension, tachycardia or hypotension, and signs of intermittent bleeding. In patients who have already undergone surgery for pancreatitis, bloody drainage along the draining tube can be a clue for intra-abdominal hemorrhage.

Radiologic findings on imaging studies of bleeding in acute and chronic pancreatitis are as follows: the presence of hematomas (Fig. 1A), hemorrhagic pseudocysts, extravasation of contrast media (Fig. 2A) or the formation of an arterial pseudoaneurysm (Fig. 3A, 4A). Among these conditions, a pseudoaneurysm is considered that it should be treated due to its risk of rupture with catastrophic consequences with mortality rate up to 60%, even if sometimes it can be clinically silent.

Kim et al categorized the findings on digital subtraction angiography as follows: contrast extravasation due to arterial rupture (Fig. 2C, 2D); pseudoaneurysm formation (Fig. 4B, 4C); and luminal irregularity. The most commonly affected artery is the splenic artery which accounts for 30% to 44% of all affected vessels, followed by the gastroduodenal artery and its branches, pancreaticoduodenal arteries, and superior mesenteric arteries.

Technique of Endovascular Treatment

Traditionally, the mainstay of endovascular treatment has been transcatheter embolization. Coils and N-butyl cyanoacrylate (NBCA), combined by microparticles such as gelatin sponge, are the most commonly used embolic materials. In many cases, the choice of embolic material is operator-dependent, and two or more different embolic materials can be combined. As is well known, each embolic material has its own properties. Liquid agents such as NBCA can be delivered to distal narrow or tortuous vessels or all potential channels that would otherwise be difficult to reach with a microcatheter. Many previously published reports stated that using NBCA as embolic material in hemorrhage, including pseudoaneurysm, has a favorable success rate and a shorter procedure time. Furthermore, NBCA polymerization with anion in the blood is not affected by the coagulation process and NBCA can be used in patients with coagulopathy. However, NBCA has been considered as a difficult embolic material because it has to be carefully injected and the catheter must be quickly removed after the injection in order to avoid adherence of the

Fig. 1. A 54-year-old female with alcoholic pancreatitis was evaluated for exacerbated abdominal pain. (A) An axial, contrast-enhanced computed tomography scan shows a focal pseudoaneurysm (arrow) at the pancreas head and with surrounding hemorrhagic fluid collection around the pancreas. (B) A superior mesenteric arteriogram shows a pseudoaneurysm (arrow) in the pancreaticoduodenal arcade. Embolization of inflow and outflow of the pseudoaneurysm was performed with microcoils (not shown). (C, D) Final superior mesenteric and celiac arteriograms show no residual pseudoaneurysm.
Fig. 2. A 57-year-old male with alleged necrotizing pancreatitis presented with hypovolemic shock. (A, B) Axial contrast-enhanced computed tomography scans show necrotizing pancreatitis with a percutaneous drainage catheter in situ. An extravasation of contrast media [arrow] is seen around the pancreas head portion. There is hemorrhagic fluid near the celiac trunk. (C) On a celiac angiogram, a pseudoaneurysm with extravasation of contrast media [arrow] from gastroduodenal artery is noted. (D) After embolization with N-butyl cyanoacrylate, there was no further active bleeding on completion angiography.

Fig. 3. A 55-year-old male with a history of alcoholic pancreatitis was evaluated for abdominal pain and hypovolemic shock. (A, B) Axial and coronal, contrast-enhanced computed tomography scans show a pseudoaneurysm (arrows) with extravasation of contrast media in the pancreas head. (C, D) On celiac and gastroduodenal arteriograms, there is a pseudoaneurysm from the gastroduodenal artery. (E) Pancreaticoduodenal branches as well as the gastroduodenal artery were successfully embolized using vascular plugs, microcoils, and N-butyl cyanoacrylate. (F) Completion angiography shows no further bleeding.
catheter tip to the vascular wall. The ratio of NBCA to iodized oil should also be carefully estimated. Microcoils have their own advantages in terms of a wide variety of coil sizes and that they can be used more accurately, thereby making controlled embolization possible. The standard principle for the embolization technique is to embolize the bleeding focus, including the pseudoaneurysm, both proximally and distally to the lesion, in order to prevent bleeding from back-flow from the collaterals (Fig. 4D, 4E). The principle of pseudoaneurysm embolization is to exclude the pseudoaneurysm from the arterial circulation. Therefore, the microcoil placement from distal to proximal from the pseudoaneurysm can frequently be used. However, it requires insertion of the catheter at the bleeding site. Moreover, this method is not always applicable in patients with small or tortuous vessels, and it is difficult to use coils when there are many efferent arteries or collateral vessels.

Recently, stent-graft placement for the exclusion of arterial rupture and pseudoaneurysms has gained popularity. The use of a stent-graft preserves blood flow to a distal organ and which can prevent end-organ ischemia. Stent-grafts are safe to use, but the necessity of a stiff and larger profile delivery system is technically more challenging to position. Some current literatures reported successful embolization by thrombin injection which was done percutaneously or via endoscopic ultrasound. The use of ethylene vinyl alcohol copolymer (Onyx; ev3, Plymouth, MN, USA), which polymerizes more slowly and has less catheter adherence than NBCA, was also reported, but in only a very limited number of patients. According to a previous report, the treatment strategy differs whether there is arterial or venous bleeding. While arterial bleeding can be managed by angiographic embolization, venous bleeding, including major venous bleeding and diffuse venous bleeding after necrosectomy or sequestrectomy can present therapeutic challenges and have a high mortality rate (50%). This can be explained by the increased difficulty in identifying and controlling venous bleeding by angiographic treatment and also by the severity of locoregional destruction associated with venous injuries. Surgery, such as packing with moist gauze and, in selected patients, emergency proximal or distal pancreatectomy, can have a major role in those patients and can sometimes be the only way to stop the fatal course.

**Clinical Outcomes and Complications**

The overall technical success rate of the endovascular treatment ranges from 84.5% to 100%, The rebleeding rate after the first endovascular treatment varies, ranging from 0% to 37% One previous report by Kim et al stated that the clinical success rate was 91.9% and that the reasons for rebleeding in the remaining three patients were recanalization of the embolized artery, development of new bleeding sites, and persistent retrograde filling of the pseudoaneurysm in which only the proximal feeding artery could be embolized owing to technical difficulties during the catheterization. Two of these patients were successfully treated by a second embolization procedure, leaving only one patient with failed hemostasis. In another report by Izaki et al., there were no episodes of repeat bleeding from a previously embolized territory, although additional bleeding from new vessels was discovered in three of nine patients (33%). Kish et al reported several reasons for failure to control hemorrhage during transcatheter embolization, including the inability to infuse the embolic material at the bleeding site, increased collateral flow to the bleeding site, recanalization of the embolized vessels, and not correctable coagulopathy.

Severe inflammation in the surrounding tissue can be one of the risk factors for recurrence. When there is pseudoaneurysm embolization, occluding both the proximal and distal segments of the artery should be performed in order to prevent rebleeding from back-flow.

A limited number of studies deal with the long-term clinical
outcome of endovascular treatment. In a report by Vander Mijnsbrugge et al., the recurrence rate was 12%, i.e., 9% with the development of a new pseudoaneurysm on a different vessel and 3% with reopening of the excluded pseudoaneurysm, all of which occurred within the first five months after embolization. Vander Mijnsbrugge et al. also stated that the estimated survival rates were 94%, 89%, and 75% after two, five, and 10 years, respectively, and without pseudoaneurysm-related patient death during the long-term follow-up period.

The most common complication has been splenic infarct which has been categorized as a minor complication due to the absence of clinical signs and requiring no major treatment, thus accounting for 10% to 50%. According to Kim et al., 8.1% of patients developed splenic abscess which is categorized as a major complication, and they required further interventional procedures such as percutaneous drainage. Complications in the spleen developed only in patients in which the splenic artery had been embolized in the distal segment adjacent to or at the splenic hilum. Other reported complications include duodenal mucosal ischemic ulceration of the duodenum, migration of microcoils, subcapsular splenic hematoma, and necrosis of cecum necessitating right hemicolectomy.

In conclusion, endovascular management is effective and safe for managing patients with pancreatitis-related bleeding. Clinical suspicion, precise diagnosis, and prompt management are critical in dealing with pancreatitis-related bleeding complications.

Conflicts of Interest

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

References

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