Endovascular treatment for delayed post-pancreaticoduodenectomy hemorrhage of unusual origin (splenic artery branch)

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ABSTRACT

Objective: The objective of this study was to investigate the method, efficacy, and safety of endovascular treatment (EVT) of delayed splenic artery branch (SAB) hemorrhage after pancreaticoduodenectomy.

Methods: From March 2019 to January 2022, all patients underwent EVT of SAB for delayed post-pancreaticoduodenectomy hemorrhage were included. Demographic, laboratory, angiographic, and clinical follow-up data were collected and analyzed.

Results: A total of eight patients were enrolled. In two patients, celiac axis angiography alone failed, but selective splenic artery (SA) angiography demonstrated the SAB bleeding; SAB erosions in four patients with recurrent bleeding were successfully detected by a second angiography; four patients underwent balloon catheter placement at the SA for temporary hemostasis and to further confirm the SAB bleeding before the subsequent EVT. Superselective embolization was performed in only one patient (12.5%; 1/8); covered stent implantation at the SA was performed in two patients (25%; 2/8); Embolization of the SA was performed in the remaining five patients (62.5%; 5/8). The technical success rate, clinical success rate, and in-hospital mortality were 100.0%, 87.5%, and 25%, respectively. No severe complications related to EVT occurred.

Conclusions: EVT of SAB for delayed post-pancreaticoduodenectomy hemorrhage is effective and safe. An awareness of the SAB as a potential bleeding source, together with appropriate endovascular procedures including selective SA angiography, repeat angiography, balloon catheter placement at the SA, and applicable hemostasis protocol, could achieve a high success rate of managing SAB hemorrhage. (J Vasc Surg Cases Innov Tech 2022;8:865-71.)

Keywords: Delayed hemorrhage; Endovascular treatment; Pancreaticoduodenectomy; Splenic artery branch

As surgeon experience and perioperative management techniques have increased, mortality rate for pancreaticoduodenectomy (PD) has decreased drastically over the years, but morbidity remains high.[1] Post-pancreaticoduodenectomy hemorrhage (PPH) occurs less frequently but has been associated with a significant increase in mortality.[2,3] Early PPH[4] occurring in the first 24 hours postoperatively is often due to technical failure or coagulopathy, generally requiring repeat laparotomy. Delayed PPH[4] occurs >24 hours postoperatively, which mainly results from vessel erosion correlated with pancreatic fistula, bile leakage, and abdominal infection.[5] Endovascular treatment (EVT) provides rapid control of acute bleeding. Many published studies have identified its efficacy and safety in the management of delayed PPH, and most of these cases involved the common bleeding sites from the stump of the gastroduodenal artery (GDA), the hepatic artery (HA), and the superior mesenteric artery (SMA).[6-8] The splenic artery branches (SABs) provide blood supply for the organs adjacent to the surgical area and could also be sources of such bleeding, although this is reported much more rarely. Bleeding from SABs may be hard to treat because of the difficulty in identification on angiogram, especially in bleeding intermission, difficulty with superselection, and also due to the rich collateral circulation that occurs through the pancreaticoduodenal arcades.[9,10] To our knowledge, to date, the data presented lack in the setting of SAB hemorrhage after PD. Herein, we report eight cases of delayed PPH to evaluate the safety and efficacy of endovascular procedures to treat the uncommon bleeding from SAB.

MATERIAL AND METHODS

Patients. This retrospective study was conducted in the Department of Interventional Radiology of Shanghai Eastern Hepatobiliary Surgery Hospital. The ethics committee approved the study. Because of the retrospective

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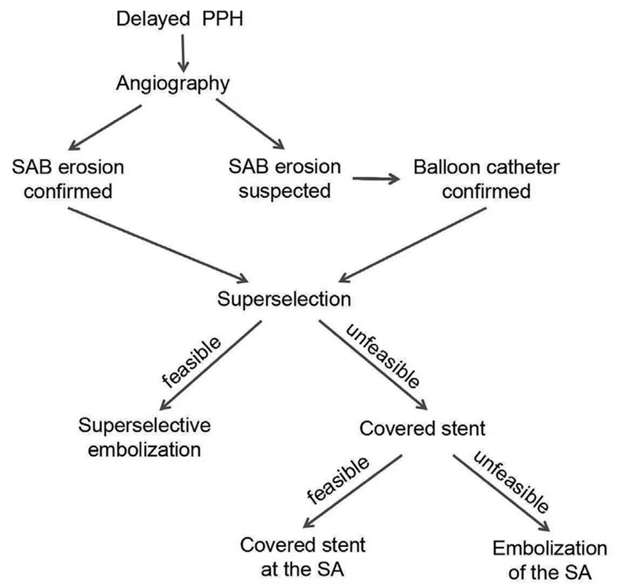

Fig 1. Flowchart depicting the selection process of endovascular procedures for managing the splenic artery branch (*SAB*) erosions. *PPH*, Post-pancreaticoduodenectomy hemorrhage; *SA*, splenic artery.

nature of this study, no written informed consent was required. PPH was defined and evaluated according to the International Study Group of Pancreatic Surgery guidelines.[4] Between March 2019 and January 2022, all patients underwent angiography for suspected delayed arterial bleeding after PD were identified in our database. SAB hemorrhage occurred in eight patients with a mean age of 62.6 years (range, 46-75 years), and these patients were enrolled in this study.

Endovascular procedures. Endovascular procedures were performed by one of five experienced abdominal interventional radiologists. A 5-F vascular sheath (Terumo Corp, Tokyo, Japan) was inserted through the common femoral artery under local anesthesia, then angiography of the celiac axis and the SMA was routinely performed to detect bleeding using a 5-F angiographic catheter (RH: Hanaco Medical Co, Tianjin, China; Yashiro: Terumo Corp, Tokyo, Japan) with an automated injection of 30 mL of iodinated contrast material at a rate of 5 mL/s with 300 psi of pressure. The branches of the celiac axis were selectively catheterized using the above-mentioned 5-F catheter or a 2.8-F microcatheter (Boston Scientific, Natick, MA) with an automated injection of 9 mL of iodinated contrast material at a rate of 3 mL/s with 500 psi of pressure when no bleeding was found. Signs of the target vessel on the angiogram included contrast media extravasation, a pseudoaneurysm, and stenosis/irregularity. The selection process of the subsequent endovascular procedures is depicted in Fig 1. In some cases, the SAB was highly suspected of the source for delayed PPH on angiogram and consistent with clinical characteristics, but its angiography was indeterminate because of disturbance of breathing movement, gastrointestinal peristalsis, or pneumatosis. After consulting with the attending surgeon, a balloon catheter (Boston Scientific) with balloon filled with contrast agent was placed at the main splenic artery (SA), and then the patient went back to the inpatient ward. If bleeding cessation lasts 1 to 3 days, the SAB hemorrhage could be confirmed and then treated by the subsequent EVT.

After identifying the bleeding site, the affected SAB was superselected using a microcatheter mentioned above. Embolization of the SAB was performed with microcoils (Cook Medical, Bloomington, IN). When the affected SAB could not be superselected, priority should be given to the implantation of covered stent at the SA. With appropriate technique, the 5-F sheath was replaced by an 8-F sheath (Terumo Corp), then a covered stent (Fluency Plus, C.R. Bard Company, Franklin Lakes, NJ) was negotiated into the SA over a 0.035-inch/260-cm stiff guidewire (Boston Scientific). The covered stent was centered on the origin of the bleeding SAB and then deployed. N-butyl cyanoacrylate (NBCA) (Compoint Medical Devices Co, Beijing, China) was chosen to embolize the SA when both the bleeding SAB could not be superselected and covered stent implantation at the SA was impossible due to the anatomic situation. In such cases, the distal main SA was embolized with interlock microcoils (Interlock Fibered IDC Occlusion System, Boston Scientific, Cork, Ireland) to prevent far distal embolization, followed by NBCA embolization including the origin of the bleeding focus and the proximal main SA. NBCA was mixed with ethiodized oil (Lipiodol, Andre Guerbet, Aulnay-Sous-Bois, France) at a ratio of 1:1 to 1:3. The ratio was mainly based on experience of the operator, by considering the polymerisation times of the mixture, the vessel size, and the flow dynamics of the main SA. The mixture was injected through the microcatheter after flushing with 5% dextrose water, and the microcatheter was promptly removed to prevent adhesion of the catheter tip to the artery wall.

At the end of the embolization or covered stent placement, repeat angiography was performed to confirm cessation of bleeding of the target artery. The puncture site was closed with an arterial closure devise or manually compressed.

Definitions. Technical success was defined as complete cessation of the SAB bleeding on the completion angiogram; clinical success was defined as absence of symptoms of recurrent hemorrhage and no requirement for additional procedures (eg, surgery, endoscopy, or EVT) within 30 days after EVT of the SAB bleeding; major complications of EVT were classified as a serious adverse event (grades 3-6) according to the reporting standards of the Cardiovascular and Interventional Radiological Society of Europe.[11]

Table I. Patient demographics and characteristics

Patient No.	Age, y/ Sex	Disease	Postoperative complications	Interval, days	Hemorrhage sign	Grade of hemorrhage	Hb, g/ dL	Sentinel bleeding	Hemorrhagic shock
1	63/F	Pan Ca	None	5	Hematemesis, melena	C	8.0	No	No
2	46/M	CBD Ca	PF	18	Hematemesis	C	5.5	No	No
3	50/F	CBD Ca	PF, AI, BL	11	Hematemesis	C	8.3	No	No
4	75/M	CBD Ca	PF, AI	11	Abdominal drain tube, hematochezia	C	7.0	No	Yes
5	72/F	CBD Ca	PF, AI	132	Operative wound	C	5.5	No	Yes
6	66/M	CBD Ca	PF, AI	22	Melena	B	7.6	No	No
7	60/F	Pan Ca	PF	9	T-tube, nasogastric tube	B	7.3	Yes	No
8	69/M	CBD Ca	PF, AI, BL	19	Abdominal drain tube, hematemesis	C	7.3	Yes	No

AI, Abdominal infection; *BL*, bile leakage; *CBD Ca*, common bile duct cancer; *Pan Ca*, pancreatic cancer; *PF*, pancreatic fistula.
Interval: interval between the initial surgery and onset of bleeding.

RESULTS

The demographic data and clinical characteristics of the eight study patients are summarized in Table I. Indications for the initial surgery were pancreatic carcinoma ($n = 2$) and common bile duct carcinoma ($n = 6$). Pancreatic leakage, bile leakage, and abdominal infection were observed in seven (87.5%), two (25.0%), and five (62.5%) patients, respectively. The average onset of bleeding was 28.4 days (range, 5-132 days) postoperatively. Clinical symptoms and signs included from gastrointestinal bleeding (T-tube, nasogastric-tube, hematemesis, hematochezia, or melena) in five patients (5/8; 62.5%), intra-abdominal bleeding (surgical wound or abdominal drain tube) in one patient (1/8; 12.5%), and both in two patients (2/8; 25.0%). Six patients had grade C and two patients had grade B hemorrhage according to the definition of the International Study Group of Pancreatic Surgery (a drop in hemoglobin serum level <3 g/dL is considered as grade B, whereas a drop >3 g/dL is grade C); two patients had sentinel bleeding within 1 day before massive hemorrhage, and hemorrhagic shock was present in two patients (12.5%); the mean hemoglobin level was 7.1 g/dL (range, 5.5-8.3 g/dL). Before the EVT of the SAB bleeding, three patients underwent endoscopy. Unfortunately, endoscopy failed in localizing the bleeding sites due to extensive blood clots in two patients (patients 2 and 3) and failed in interventionally treating bleeding at the gastroenteric stoma in one patient (patient 1).

The endovascular procedures and outcomes are summarized in Table II. In two patients (patients 2 and 8) celiac axis angiography alone failed, but selective SA angiography managed to demonstrate the bleeding in the SAB. Among these eight patients, one patient (patient 2) had no visible involved artery on the initial angiography, then converted to open surgical hemostasis, but also failed to identify any target vessels; rebleeding occurred in this patient, and the SAB erosion was successfully identified by a second angiography. Three patients (patients 1, 4, and 8) had clinical suspicion of rebleeding after the initial embolization of the affected arteries (two for SMA branch bleeding, one for left gastric artery bleeding); a second angiography was performed in these three cases, and bleeding from the SAB was finally revealed, despite the embolized arteries at the initial angiography being excluded without evidence of rebleeding. The remaining four patients (patients 3, 5, 6, and 7) were discovered with SAB bleeding on the initial angiography.

In this cohort, four patients (patients 2, 3, 6, and 7) underwent balloon catheter placement at the main SA for hemostasis and to further confirm the SAB bleeding before EVT. Regarding the hemostatic techniques, superselective embolization of the bleeding SAB was only performed in one patient (patient 1) using microcoils (Fig 2); in two of eight patients (patients 2 and 3), covered stent implantation at the main SA (mother artery of the bleeding branch) successfully ceased extravasation (Fig 3); embolization of the main SA was performed using NBCA and interlock microcoils in the remaining five patients (patients 4-8) (Fig 4). The SAB bleeding foci were all excluded successfully on the completion angiography, resulting in a technical success rate of 100%. Despite successful cessation of bleeding of the SAB on angiogram, one patient (patient 5) died 1 day later due to persistent hemorrhage secondary to multiple organ dysfunction syndrome. The remaining seven patients showed no evidence of recurrent bleeding after EVT of the SAB erosions, resulting in a clinical success rate of 87.5% (7/8). Among these seven patients with clinical success, one patient (patient 6) died at 9 days after EVT due to multiorgan failure caused by sepsis accompanied by uncontrolled pancreatic fistula and severe abdominal infection; the other six patients were discharged successfully, thus the in-hospital mortality of the cohort was 25%

Table II. Summary of endovascular procedures and outcomes

Patient No.	SABH by initial angiography	SABH by CA angiography	Balloon catheter placement	Material and technique	Technical/ Clinical success	Outcome (in hospital)	Outcome (follow-up)
1	No (LGAH)	Yes	No	Selective coil embolization (SAB)	Yes/Yes	Alive	Alive
2	No	No	Yes	Covered stent (SA)	Yes/Yes	Alive	Died (neoplasm)
3	Yes	Yes	Yes	Covered stent (SA)	Yes/Yes	Alive	Alive
4	No (SMABH)	Yes	No	Coil and NBCA embolization (SA)	Yes/Yes	Alive	Alive
5	Yes	Yes	No	Coil and NBCA embolization (SA)	Yes/No	Died (bleeding)	_
6	Yes	Yes	Yes	Coil and NBCA embolization (SA)	Yes/Yes	Died (sepsis)	_
7	Yes	Yes	Yes	Coil and NBCA embolization (SA)	Yes/Yes	Alive	Alive
8	No (SMABH)	No	No	Coil and NBCA embolization (SA)	Yes/Yes	Alive	Alive

CA, Celiac axis; *LGAH*, left gastric artery hemorrhage; *NBCA*, N-butyl cyanoacrylate; *SA*, splenic artery; *SABH*, splenic artery branch hemorrhage; *SMABH*, superior mesenteric artery hemorrhage.

Fig 2. A 63-year-old woman (patient 1) with recurrent bleeding 2 days after embolization of the left gastric artery. **a,** Celiac axis angiography showed a leakage (*arrows*) of contrast agent from the stenosing/irregular splenic artery branch (SAB) and the embolized left gastric artery (*solid arrows*) being excluded without evidence of rebleeding; **b,** Selective splenic artery (SA) angiography further confirmed the active bleeding from the branch (*arrows*) arising from the proximal SA; **c,** After microcoil embolization (*arrow*) of the SAB, the completion angiogram showed the cessation of the active bleeding.

(2/8). The mean follow-up was 10 months (range, 4-26 months) after EVT in the six alive patients. During this period, one patient (patient 2) died secondary to neoplasm. No patients had severe complications like necrotizing pancreatitis, gastric ischemia, or splenic abscess during the follow-up period.

DISCUSSION

EVT as a feasible option in the management of delayed PPH is well-documented to treat the common bleeding sites. Nonetheless, it was proposed that ignorance of bleeding from unusual sources, such as adrenal artery, ileocolic artery, and the dorsal pancreatic artery (DPA) (the most common origin of the DPA is the proximal SA), would increase the chances of technical and/or clinical failures that necessitate additional procedures such as reoperation.[9,10,12-14] The pancreas is vascularized by splenic, gastroduodenal, and superior mesenteric arteries, and these mentioned vessels send numerous branches into the different parts of pancreas and adjacent organs.[15,16] In general, SA gives out pancreatic branches that supply the pancreatic body and tail, and gastric branches that supply the fundus of stomach.[16] There remains a paucity of reports describing delayed SAB bleeding after PD in detail, the subsequent endovascular results, and the survival prognosis of the patients, with the reports being limited to several case reports and small case series.[9,10,12,17,18] This present study reports the outcomes of endovascular procedures to treat the SAB erosions for delayed PPH.

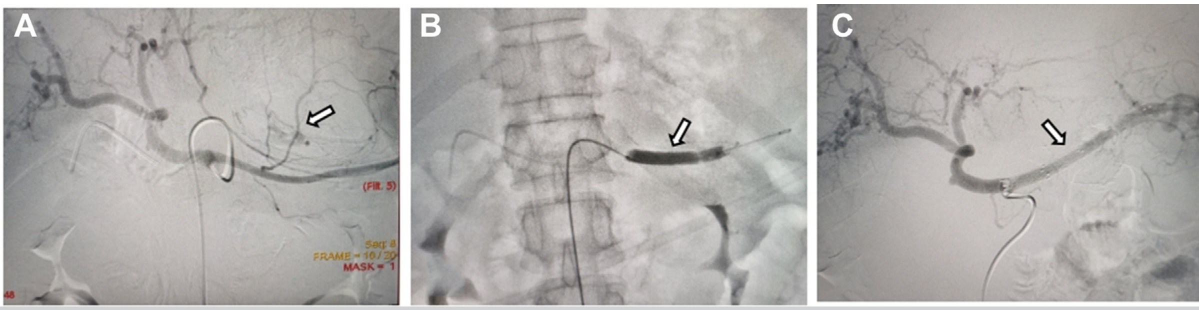

Fig 3. A 46-year-old man (patient 2) with no involved artery identified on the initial angiogram and reoperation; recurrent bleeding occurred 7 days later. **a,** Celiac axis angiography showed a leakage (*arrows*) of contrast agent suggesting an extravasation from the SAB; **b,** Balloon catheter placement (*arrows*) at the main splenic artery (SA) for temporary hemostasis and to further confirm the splenic artery branch (SAB) bleeding; **c,** After failed attempts of superselection of the bleeding branch, covered stent implantation (*arrows*) at the main SA successfully isolated the blood supply of the bleeding SAB and potential collateral arteries.

Fig 4. A 72-year-old woman (patient 5) with bleeding from surgical wound after pancreaticoduodenectomy (PD). **a,** Celiac axis angiography showed a leakage (*arrows*) of contrast agent suggesting an extravasation from the splenic artery branch (SAB); **b,** Selective splenic artery (SA) angiography further confirmed the active bleeding from the branch (*arrows*) arising from the proximal SA; **c,** After embolization (*arrows*) of the main SA with N-butyl cyanoacrylate (NBCA) and interlock microcoils, the completion angiogram showed NBCA flowed into the bleeding SAB and potential arterial collateral routes to the hemorrhage spot, indicating the complete cessation of the active bleeding.

Data reveals that, in two of eight patients (25%), celiac axis angiography alone failed, but selective SA angiography managed to demonstrate the bleeding in the SAB. Kortney[9] also reported two cases with delayed PPH where the culprit artery was found on celiac axis angiography, but selective SA angiography finally identified that the DPA from the proximal portion of the SA was the bleeding focus. Therefore, it is important for interventional radiologists to be familiar with the fact that the SAB bleeding exists, and selective SA angiography is a crucial step. In our study, although no SAB bleeding was identified on the initial angiography in 50% of patients (4/8), rebleeding due to SAB erosions was successfully managed by a second angiography, proving the repetitive approach could increase the success rate of EVT for rebleeding patients. In addition, four patients (50%; 4/8) successfully underwent balloon catheter placement before the subsequent EVT. It indicates that balloon catheter placement at the main SA is a useful method for confirming the SAB bleeding and avoiding the risks associated with embolization of non-target vessels.

Table III provides a review of the literature to summarize the interventional techniques for delayed SAB hemorrhage after PD. Superselective catheterization of the bleeding SAB is difficult due to the proximal origin of the SA, anatomical situations (tortuosity, length, acute angulation), and vasospasm caused by massive blood loss or latrogenic procedures. In this situation, reoperation may be an alternative method, but it often leads to longer hospital stays and higher overall mortality compared with EVT.[19,20] Kim[10] reported a direct percutaneous NBCA embolization of pseudoaneurysm of supplied by the fine pancreatic arteries arising from the SA after failed attempts of superselection. However, the direct percutaneous embolization is technically challenging and only confirmed feasible in bleeding caused by aneurysms or pseudoaneurysms with a relatively large size.[21] In our study, superselective embolization by microcoils was successfully performed in only one patient

Table III. Literature summary of interventional techniques for delayed splenic artery branch (*SAB*) hemorrhage after pancreaticoduodenectomy (PD)

Study	No. patients	Target artery origin from SA	Material and technique	Clinical success	Complication
Zhou et al 2013[17]	1	GPA	Selective gel foam embolization (SAB, n = 1)	Yes	None
Kamada et al 2021[18]	1	DPA	Selective coil embolization (SAB, n = 1)	Yes	None
Kim Y et al 2019[9]	2	DPA	Selective coil embolization (SAB, n = 1) Coil embolization (SA, n = 1) (SA)	Yes	None
Alhazemi et al 2020[12]	3	DPA	Selective coil/NBCA embolization (SAB, n = 2) Coil embolization (SA, n = 1)	Yes	None
Kim R et al 2014[10]	1	DPA	Percutaneous NBCA embolization of PSA (n = 1)	Yes	None

DPA, Dorsal pancreatic artery; *GPA*, great pancreatic artery; *NBCA*, N-butyl cyanoacrylate; *PSA*, pseudoaneurysm; *SA*, splenic artery.

(12.5%; 1/8), proving the difficulty of the SAB embolization. In addition, superselective embolization of the SAB may cause technical and/or clinical failure due to multiple fine vessels communicating with the bleeding sites. Stent implantation has been revealed to be effective for treating hemorrhage from GDA stump or pseudoaneurysms arising from HA/SA while preserving vascular patency.[7,22,23] To our knowledge, to date, no studies have described the use of covered stent implantation to set delayed SAB hemorrhage after PD. Herein, we reported the data of two patients receiving covered stent placement at the SA that isolated the blood supply of the SAB and successfully ceased the artery bleeding. However, stent implantation was impossible in the remaining five patients because of the anatomic situation of the SA; then a combination of interlock microcoils and NBCA were used. This combination allows interlock microcoils placement distal to the origin of the bleeding SAB to prevent distal non-target embolization and subsequent NBCA injection to cover the bleeding origin and more proximal portion of the SA. Similar studies[9,12] reported embolization of the main SA using coils to control DPA (arising from the SA in these cases) hemorrhage in two cases, indicating that the main SA embolization is a valuable alternative endovascular procedure for SAB hemorrhage after failed attempts of superselection or stent implantation.

Technical success was finally achieved in all patients (8/8), and the clinical success rate was 87.5% (7/8), which are comparable to these reports on EVT of the common affected arteries for delayed PPH.[24-26] The patient with clinical failure died of prolonged hemorrhage that may have been caused by multiple vessel erosions including intravenous due to severe abdominal infection. Unfortunately, no additional procedures such as repeat angiography or reoperation was conducted to identify the persistent bleeding sites because the patient was in poor physical condition. No severe procedure-related complications occurred in this cohort. Although embolization of the main SA for acute hemorrhage is generally considered to be safe, some studies have reported on necrotizing pancreatitis and splenic abscesses.[27,28] It indicates that a thorough knowledge of the potential of the common techniques and their limitations is required before undertaking the main SA embolization to treat SAB bleeding.

Several major limitations of the study include that we assessed a relatively low number of specimens, the design was retrospective, no systemic angiographic or CT examinations were performed during follow-up to identify the fate of the spleen following embolization, and the fact that the follow-up period differed widely. These limitations should be taken into account in future studies.

In conclusion, EVT is safe and effective to treat delayed SAB hemorrhage after PD. An awareness of the SAB as a potential bleeding source, together with the appropriate endovascular procedures, including selective SA angiography, repeat angiography, balloon catheter placement, and applicable hemostatic techniques, could achieve a high success rate of managing delayed PPH.

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