Article published online: 2023-11-13

Endovascular Management of Postoperative Hemorrhage after Pancreaticoduodenectomy

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Arab J Intervent Radiol 2023;7:100–106.

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Abstract

Objective The aim of the study was to assess the safety and efficacy of endovascular management for postpancreaticoduodenectomy hemorrhage.

Materials and Methods A retrospective analysis of patients who underwent endovascular management for hemorrhage after pancreatic surgery between January 2015 to December 2020 was performed. Patient demographics, clinical presentation, angiography findings, endovascular procedure, technical success, clinical success, and complications were assessed.

Results Seventeen patients, comprising 14 (82.4%) males and 3 (17.6%) females, aged 37 to 68 years underwent endovascular management for postpancreatectomy hemorrhage. Patients presented with hemorrhage on their postoperative days 4 to 22 (mean: 9.8th day; median: 8th day); the presentation was with extraluminal hemorrhage in 11 patients (64.7%) and intraluminal hemorrhage in 6 patients (35.2%). The gastroduodenal artery (GDA) stump (10 patients, 58.8%) was the most commonly involved artery. The majority of cases were treated using coils as embolizing agents (13/17 patients, 76.5%). The technical and clinical success rates were 100%. The complication rate was 5.9% (1/17) and the mortality rate was 11.8% (2/17). The relaparotomy rate was 23.5% (4/17); however, none of the relaparotomy was for hemorrhage.

Conclusion Endovascular treatment provides a minimally invasive, safe, and effective method for the management of pancreaticoduodenectomy hemorrhage.

Keywords
- endovascular
- gastroduodenal artery
- interventional radiology
- postpancreaticoduodenectomy hemorrhage

Introduction

Pancreatic surgery remains one of the more challenging surgeries with high rates of postoperative morbidity and mortality. The perioperative mortality following pancreatic surgery has reduced over the past few decades to below 5%.[1,2] However, the overall perioperative morbidity rates after pancreatic surgery are still high being reported as 18 to 46% across studies.[3–5]

Postpancreatectomy hemorrhage (PPH) is one of the most significant complications after pancreatic surgery increasing mortality and morbidity. The International Study Group of Pancreatic Surgery (ISGPS) has proposed the term "postpancreatectomy hemorrhage" as the uniform descriptor for all postoperative episodes of hemorrhage. PPH has been classified based on three criteria: (1) time of onset, (2) location and cause, and (3) severity as described in ►**Table 1**.[6]

article published online
November 13, 2023

DOI https://doi.org/10.1055/s-0043-1772256.
ISSN 2542-7075.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Table 1 The International Study Group of Pancreatic Surgery (ISGPS) proposed classification of postpancreatectomy hemorrhage (PPH)

Time of onset	Early	<24 h after the end of the index operation
	Late	>24 h after the end of the index operation
Location	Intraluminal	Intra-enteric, e.g., anastomotic suture line at the stomach or the duodenum, or pancreatic surface at anastomosis, stress ulcer, and pseudoaneurysm
	Extraluminal	Extra-enteric, bleeding into the abdominal cavity, e.g., from arterial or venous vessels, diffuse bleeding from resection area, anastomosis suture lines, and pseudoaneurysm
Severity	Mild	Hb drop <3 g/dL, mild clinical impairment, no need for reoperation or interventional angiographic embolization; endoscopic treatment of anastomotic bleeding
	Severe	Blood loss with Hb drop >3 g/dL, significant clinical impairment, or need for invasive treatment

The mortality rates after pancreatic surgery have significantly reduced over time, but the postoperative morbidity rates continue to remain high. Earlier these postoperative complications were managed primarily with surgery (relaparotomy); however, there has been an increasing role of interventional radiology (IR) in managing these postpancreatic surgery complications with minimally invasive techniques.

Materials and Methods

Patient Characteristics

Local institutional review board approval was obtained, and informed consent was waived for this type of study. Retrospective analysis of 17 consecutive patients who underwent endovascular management for hemorrhage after pancreaticoduodenectomy between January 2015 to February 2020 was performed to assess the safety and efficacy. The ISGPS definition was used to define and classify late PPH. All the patients who underwent endovascular intervention to control hemorrhage were included in the study. The electronic medical records of patients were reviewed, and demographic, clinical, treatment, final histology, and follow-up details were collected.

Preprocedure Investigations

Routine blood investigations including complete blood count and liver and renal function tests were performed in all patients. Computed tomography (CT) angiography was performed in 6 of these 17 patients, which revealed active hemorrhage or pseudoaneurysm.

Procedure

The endovascular interventions were performed through a right common femoral artery approach in all the patients. The celiac artery and superior mesenteric artery (SMA) were cannulated and selective angiography performed. Superselective catheterization of the common hepatic artery, splenic artery, gastroduodenal artery (GDA), left gastric artery, and branches of the SMA were performed with a 2.9-Fr microcatheter (Progreat, Terumo Medical Inc.). The angiography images were reviewed for the presence of active extravasation, pseudoaneurysm, and vessel wall irregularity. The vascular abnormalities were treated either by embolization or by stent graft placement. The source of bleeding identified on angiography was treated with embolizing agents like coils, glue: lipiodol, stent graft, or a combination depending on the source artery and anatomic location of the bleeding (►**Figs. 1**–**5**). In our study, the stent grafts used were GraftMaster (Abbott Vascular) and Fluency (Bard). The patients with stent graft placement were kept on anticoagulation with unfractionated heparin, and antiplatelet (aspirin 300-mg loading dose followed by 75 mg once a day) was initiated before the planned discharge from the hospital. Unfractionated heparin has the

Fig. 1 (**A**) Celiac angiogram with Judkin's right (JR) catheter showing pseudoaneurysm (*blue arrow*) arising from the gastroduodenal artery (GDA) stump. (**B**) Poststent graft (4 × 26 mm) insertion, celiac angiogram showing no filling of pseudoaneurysm with patent right hepatic artery.

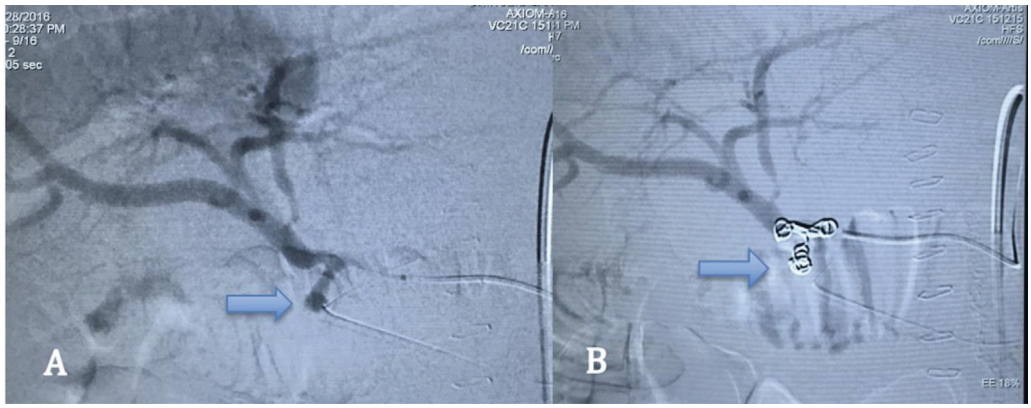

Fig. 2 (**A**) Hepatic angiogram with microcatheter showing pseudoaneurysm (*blue arrow*) arising from the gastroduodenal artery (GDA) stump. (**B**) Postembolization with coils in the stump as well as the hepatic artery segment at the level of the stump, hepatic angiogram showing no filling of pseudoaneurysm (blue arrow).

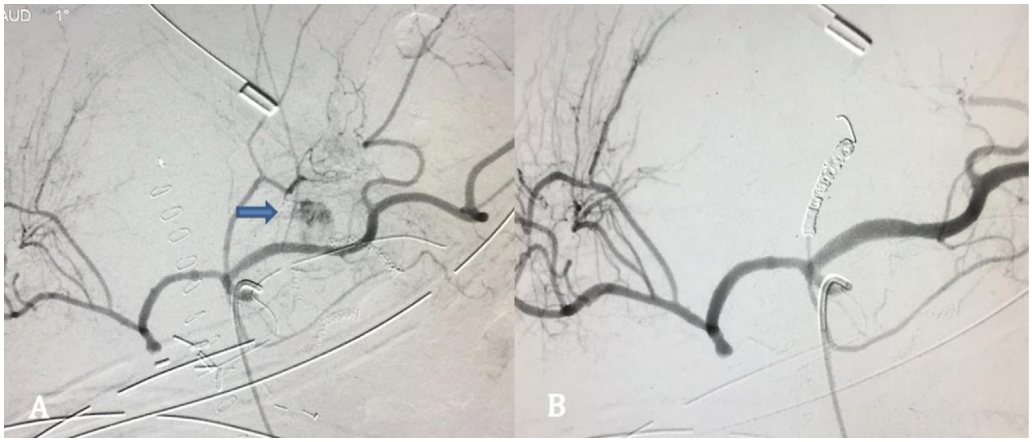

Fig. 3 (**A**) Celiac angiogram with a Cobra (C2) catheter showing active bleed (*blue arrow*) from the branch of the left gastric artery. (**B**) The left gastric artery was embolized with microcoils: celiac angiogram showing no active bleed postembolization.

advantage of having short duration of action, dose titration with activated partial thromboplastin time (APTT) monitoring, and reversibility with protamine that can be utilized if the patient rebleeds or has to undergo relaparotomy.

Technical success was defined as the cessation of contrast extravasation or exclusion of pseudoaneurysm from the vasculature. Clinical success was defined as control of hemorrhage, that is, cessation of hematemesis/melena or conversion of drain output to nonhemorrhagic fluid with no rebleeding at least 14 days after the procedure. All the patients were evaluated for postprocedural complications like bowel ischemia, hepatic infarction and hepatic failure, and hepatic and splenic abscess.

Results

A total of 17 patients who underwent endovascular management for postpancreatic surgery hemorrhage were included in the retrospective analysis. Follow-up was done at 4 to 6 weeks after discharge from the hospital. ►**Table 2** shows a summary of the patient demographics.

There were 14 (82.4%) males and 3 (17.6%) females with age ranging from 37 to 68 years (mean: 51.5 years; median: 50 years). Most of the patients were operated for pancreatic adenocarcinoma (12 patients, 70.6%). Patients presented with hemorrhage on their postoperative days 4 to 22 (mean: 9.8th day; median: 8th day). Anastomotic leak from the pancreatic anastomosis was present in 10 of the 17 patients (58.8%).

The most common site of bleeding identified on digital subtraction angiography (DSA) was the GDA stump in 10 patients (58.8%), while in the rest of the patients, these were the left gastric artery (2 patients, 11.8%), middle colic artery (2 patients, 11.8%), splenic artery (1 patient, 5.9%), replaced right hepatic artery (1 patient, 5.9%), and the first jejunal branch of the SMA (1 patient, 5.9%). On the ISGPS severity, there were 7 (41.2%) grade B and 10 (58.8%) grade C bleedings.

The majority of patients were treated with coils as embolizing agents being utilized in total 13 patients (76.5%). In three patients (17.6%), coils were used with N-butyl cyanoacrylate glue:lipiodol; in one patient (5.9%), a combination of

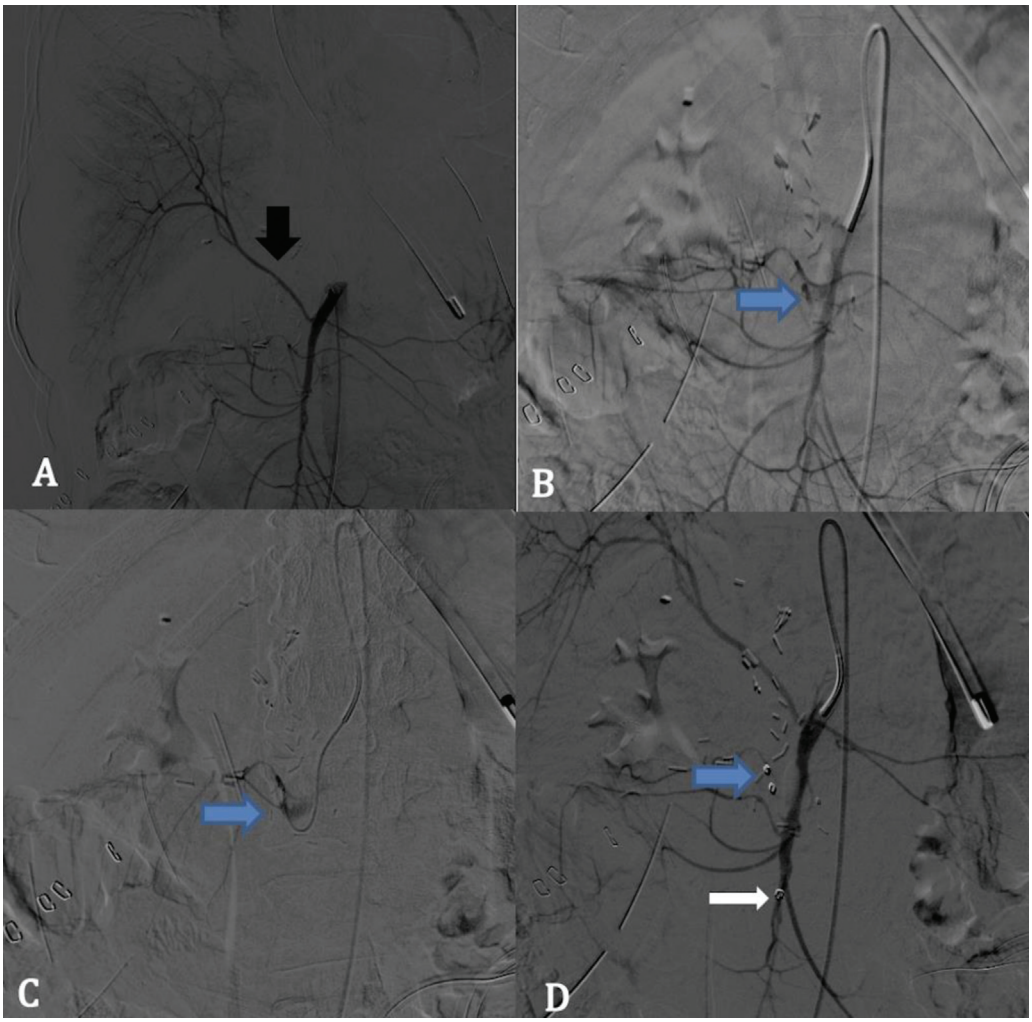

Fig. 4 (**A**) Superior mesenteric artery (SMA) angiogram showing no active bleed with replaced right hepatic artery (*black arrow*). (**B**) SMA angiogram with a Simmons (Sim2) catheter showing irregularity and pseudoaneurysm arising from the middle colic artery (blue arrow). (**C**) Superselective cannulation of the middle colic artery and active bleeding confirmed (blue arrow). (**D**) Postembolization with microcoils, SMA angiogram showing no active bleed with complete occlusion of middle colic artery (blue arrow). Also, a coil is seen in the ileal artery (*white arrow*) which had inadvertently embolized from the stump of the middle colic artery.

coils with stent graft was used. In three patients (17.6%), only stent grafts were used to reconstruct the bleeding vessel and control hemorrhage (►**Table 3**).

The outcomes are summarized in ►**Table 4**. The technical and clinical success rates were 100%.

The mortality rate was 11.7% (2 of 17 patients); one of the patients succumbed to sepsis and another with pulmonary embolism and severe acidosis.

No major postprocedural complications related to endovascular treatment were seen. One of the patients (5.9%) had few areas of hepatic infarction with asymptomatic elevation of liver enzymes; this patient underwent common hepatic artery coiling for GDA stump aneurysm. None of the patients developed bowel ischemia despite one patient having nontarget embolization with a coil embolizing into the ileal branch of the SMA while embolizing the middle colic artery (►**Fig. 4D**).

Relaparotomy was performed in four patients (23.5%) for revision of anastomosis or peritoneal wash for infection control and for blood clots for evacuation. Additional interventional procedures were required in 11 patients (64.7%), pigtail drain for abdominal collection in 5 patients (29.4%), percutaneous transhepatic biliary drainage (PTBD) in 3 patients (17.6%), and pigtail drain with PTBD in 3 patients (17.6%).

Discussion

The reported PPH rates ranged from 5 to 12% across studies[7,8]; however, it accounts for 11 to 38% of all mortality, which highlights its significant impact on patient survival.[4,9] The cause of early PPH is attributed to technical failure of appropriate hemostasis during the surgery or any underlying perioperative coagulopathy; late PPH occurs as a consequence of surgical complications (e.g., erosion of a peripancreatic vessel secondary to pancreatic fistula, infection resulting in intraabdominal collection or abscesses, anastomotic site ulceration, or due to an arterial pseudoaneurysm that has developed).[10–12] While early hemorrhage is managed with relaparotomy, the management of delayed PPH

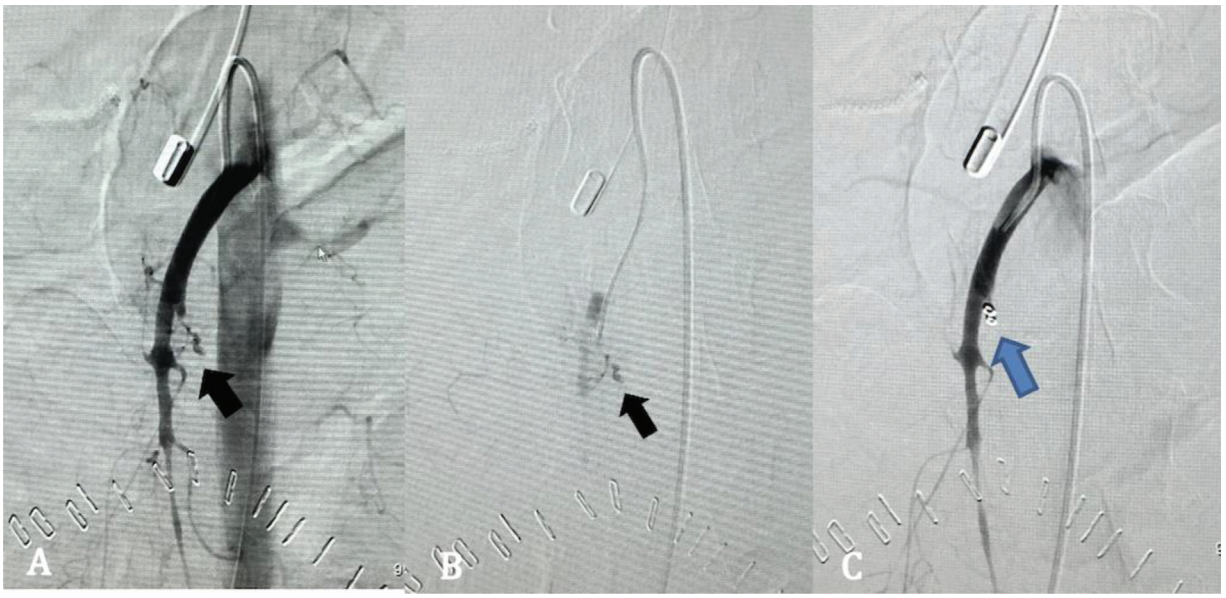

Fig. 5 (**A**) Superior mesenteric angiogram showing irregularity and pseudoaneurysm arising from the first jejunal artery (black arrow). Spasm of the entire vasculature noted. (**B**) Superselective cannulation with a microcatheter and angiogram showing the pseudoaneurysm (black arrow). (**C**) Superior mesenteric artery (SMA) angiogram showing no active bleed or filling of pseudoaneurysm after embolization with microcoils (blue arrow).

Table 2 Patient demographics and clinical details

No. of patients	17
Male:female	14: 3
Age (y)	37–68 (median: 50)
Primary diagnosis	
Pancreatic adenocarcinoma	12 (70.6%)
Distal CBD carcinoma	03 (17.6%)
IPMN	01 (5.9%)
Chronic pancreatitis	01 (5.9%)
Clinical presentation	
Postoperative day	4–22 (median: 8)
Extraluminal hemorrhage	11 (64.7%)
Intraluminal hemorrhage	06 (35.2%)
Hemodynamic instability	15 (88.2%)
Pancreatic leak	10 (58.8%)
Bile leak	05 (29.4%)

Abbreviations: CBD, common bile duct; IPMN, intraductal papillary mucinous neoplasm.

Table 3 Bleeding source as identified on angiography with endovascular intervention

Source artery	No. of patients (%)
Gastroduodenal artery (GDA) stump	10 (58.8%)
Left gastric artery	2 (11.8%)
Middle colic artery	2 (11.8%)
Splenic artery	1 (5.9%)
Replaced right hepatic artery	1 (5.9%)
First jejunal branch of the SMA	1 (5.9%)
Endovascular intervention	
Coils	9 (52.9%)
Stent graft	3 (17.6%)
Coils with NBCA (glue:lipiodol)	3 (17.6%)
Coils with stent graft	1 (5.9%)
NBCA (glue:lipiodol)	1 (5.9%)

Abbreviations: NBCA, N-butyl-2-cyanoacrylate; SMA, superior mesenteric artery.

varies as per the individual center protocols and expertise available. There has been a growing role of interventional radiologists in managing delayed PPH through endovascular methods. Angiography and embolization have proven to be a much less invasive therapeutic tool as compared with laparotomy, providing control of bleeding with less morbidity, making it a part of the first-line treatment for delayed PPH.[13,14] DSA can successfully identify the bleeding site in 70 to 90% of the cases; however, there can be negative angiography due to venous source of bleeding or intermittent nature of bleeding.[7,15]

In our study, all the 17 patients with delayed PPH responded well to endovascular management with 100% technical and clinical success rates. Various studies have demonstrated high technical success rates with endovascular therapies ranging from 83 to 100%.[16–18] There were no instances of rebleeding identified in the treated patients in our study; however, rebleeding rates from 7% to as high as

Table 4 Outcomes

Outcome	No. of patients (%)
Technical Success	17 (100%)
Clinical Success	17 (100%)
Mortality	2 (11.8%)
Relaparotomy	4 (23.5%)
Percutaneous drainage of abdominal collection	8 (47.1%)
PTBD for biliary diversion	6 (35.3%)
Complications	1 (5.9%)

Abbreviation: PTBD, percutaneous transhepatic biliary drainage.

25% have been reported. A study by Ching et al[19] recognized rebleeding rates of 25%, but the rebleed was from a new vascular source in 80% of these. The recurrence of bleeding is usually related to persistence of the triggering factors (i.e., pancreatic/bile leak, persistent infection), which implies the importance of addressing the underlying cause as a measure to prevent rebleeding.

The mortality rate in our study was 11.7% (2/17); one patient died due to sepsis and another from pulmonary embolism and severe acidosis. None of the mortalities were related to interventional procedures but followed the expected postsurgical complications. Roulin et al concluded that there was no significant difference between IR and laparotomy in terms of complete hemostasis (80 vs. 76%), but a significant decrease in mortality in IR versus laparotomy (22 vs. 47%).[20] Relaparotomy was performed in 4 of 17 patients; it involved peritoneal wash for sepsis control and blood clot evacuation in 2 patients (11.7%), while 2 patients (11.7%) required revision of anastomosis.

Sentinel bleed was seen in five patients from the drain (29.4%). Sentinel bleeding after pancreatoduodenectomy is indicative of local sepsis and possible dehiscence of anastomosis leading to pseudoaneurysm formation. The presence of sentinel bleeding followed by significant hemorrhage is found to be associated with a mortality rate of over 50%.[7,21] Thus, sentinel bleed is considered an important indicator of underlying significant pathology and requires prompt evaluation with either CT angiography or DSA. In our series, one patient (1/5, 20%) with sentinel bleed died.

The GDA stump is the most commonly identified bleeding vessel in PPH. In our study, also, the GDA stump was the most common site of hemorrhage in 10 (58.8%) of cases. This observation has led to modification of standard surgical technique, with surgeons performing distal ligation of the GDA rather than flush ligation; this provides the interventional radiologist with a longer GDA stump to accommodate placement of coils. Placement of a radiopaque clip also helps in the fast localization and identification of the site of the GDA stump.[22] In the cases with higher grade of hemorrhage, prophylactic coiling of the GDA stump despite the lack of definitive angiographic proof of the bleeding site has also been described because PPH was clinically suspected to originate from the GDA.[7] This prophylactic embolization of GDA stump is practiced because the bleeding may be masked by vasospasm, compression from surrounding hematoma, or due to the effect of inotropic medications.

The majority of patients in our study were treated with coils as embolizing agents (13 patients, 76.5%). The rest of the patients were treated with a combination of glue and coils (3 patients, 17.6%) and stent grafts (4 patients, 23.5%). There is no universal rule to the use of these embolizing agents or stent grafts for treating PPH. Embolizing agents are usually used more commonly than stent grafts, and the choice between the embolizing agents depends on angiographic findings, location of bleeding site, possibility to get across the bleeding site, and operator experience with these agents. Coils are safe with more control during deployment (especially detachable/interlock coils) compared with glue. There is risk of nontarget embolization with glue; however, this varies with operator experience. Coils are preferred when there is a single feeding vessel that can be sacrificed or to "trap" the pseudoaneurysm/bleeding vessel if one can get across the bleeding site. Liquid embolic agent (glue) is used to embolize when one cannot cross the bleeding site to trap or to embolize small collaterals that cannot be directly catheterized.[23] Stent grafts are mainly used to exclude the bleeding site/pseudoaneurysm from vasculature when the available stump is too small to accommodate coils or when the artery itself is diseased. These have the advantage of preserving the hepatic blood flow when the common hepatic artery is involved by reconstructing the artery; however, in case a stent graft is not available, parent artery occlusion can be done to control life-threatening hemorrhage. However, a study by Sato et al[24] found that sacrifice of the common hepatic artery is associated with increased risk of hepatic complications like hepatic failure and hepatic abscess with the risk of complications being eight times more in the absence of hepatic collateral pathways involving the hepatic, replaced, or accessory hepatic arteries.

Anastomotic leak from the pancreatic anastomosis was present in 10 of the 17 patients (58.8%). Das et al[8] concluded that pancreaticojejunostomy (PJ) leak was more common in the hemorrhage group compared with the nonhemorrhage group (41 vs. 20.7%), making PJ leak an independent risk factor for PPH. Yekebas et al[7] had an even more significant correlation with 39% patients with PPH having proven fistula prior to PPH, while in the entire cohort of 1,669 cases, the overall pancreatic fistula rate was 9% ($p < 0.001$). There were a total of 14 additional interventional procedures required in 11 patients (64.7%), percutaneous drain for abdominal collection in 8 patients (29.4%), and PTBD in 6 patients (17.6%). Among these 11 patients, 3 patients had both percutaneous drainage and PTBD. As already discussed, it is of utmost importance to investigate and address the underlying cause of PPH to prevent rebleeding. In a study evaluating the role of IR procedures to manage complications after pancreaticoduodenectomy, repeat surgery was avoided in 90% of the patients receiving IR management for these complications.[25] Another study by Sanjay et al[26] also concluded that many significant complications (PPH, pancreatic fistula, intra-abdominal abscess) can be

managed by IR; surgery is still required in a small percentage (2.5%) of patients.

This study is limited in being retrospective with a small sample size. Also, this is not a direct comparative study and comparison of interventional management with surgery was done using historical data from other studies.

Conclusion

Endovascular treatment provides a minimally invasive, safe, and effective method for the management of PPH. A high technical and clinical success, low rebleeding rates, low complication, and low mortality rates in this study provide support for endovascular treatment in PPH and should be considered as the preferred treatment approach for PPH. It is important to address the underlying cause of PPH like pancreatic fistula or abscess to prevent rebleeding.

Authors' Contribution

R.G. was responsible for conceptualization, data curation, and methodology. M.S. was responsible for formal analysis, writing of the original draft, and resources and literature review. A.G. was responsible for the software. Writing and review and editing were done by K.G. and R.G.

Conflict of Interest

None declared.

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