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ORIGINAL ARTICLE

Management and outcomes of pseudoaneurysms presenting with late hemorrhage following pancreatic surgery: A six-year experience from a tertiary care center

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Abstract

Background/Purpose Late hemorrhage following pancreatic surgery is associated with significant morbidity and mortality. Pseudoaneurysm (PSA) is an important source of late hemorrhage, which is effectively and safely managed by embolization. We aim to retrospectively review the outcomes of embolization for pseudoaneurysms causing late post-pancreatectomy hemorrhage over a period of six-years at our tertiary care center.

Methods Between 2014 and 2020, 616 pancreatic surgeries were performed and 25 patients had late hemorrhage (occurring > 24 hours post-operatively). The clinical parameters related to late hemorrhage, associated complications, embolization details, treatment success and their short-and long-term outcomes were analyzed.

Results Sixteen of 25 patients had PSA on digital subtraction angiography. Embolization was performed in these patients with technical and clinical success rates of 94.1% and 100%, respectively. Compared to patients without PSA, patients with PSA had significant hemoglobin drop (2.5 g/dL vs. 1.5 g/dL, $p = 0.01$), higher incidence of sentinel bleed (50% vs. 11.1%, $p = 0.05$) and lower requirement for surgery for bleeding (0% vs. 44.4%, $p = 0.02$). Clincally relevant postoperative pancreatic fistula and bile leak were seen in 72% and 52% of patients, respectively. Eight of these embolized patients died due to sepsis. The long-term outcome was good, once the patients were discharged.

Conclusion Late hemorrhage after pancreatic surgery was associated with high mortality due to complications such as pancreatic fistula and bile leak. Sentinel bleeding was an important clinical indicator of PSA. Angiographic embolization is safe and effective without any adverse short or long-term outcomes.

Keywords Angiographic embolization · Delayed pancreatic hemorrhage · Interventional radiology · Pancreatic surgery · Postoperative pancreatic fistula · Post-pancreatectomy hemorrhage · Pseudoaneurysm

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Bullet points of the study highlights

What is already known?

- Delayed hemorrhage after pancreatic surgery, often due to a pseudoaneurysm, is associated with significant morbidity and mortality.

What is new in this study?

- Evaluation of the incidence of delayed hemorrhage and of pseudoaneurysms following pancreatic surgeries and the endovascular management of pseudoaneurysms in a large patient cohort in a tertiary care center.

What are the future clinical and research implications of the study findings?

- The study emphasizes that pancreatic fistula and bile leak increase the risk of late post-pancreatectomy hemorrhage and embolization is an effective treatment option in the presence of pseudoaneurysm. This knowledge is critical in defining a prompt imaging protocol and radiological intervention whenever necessary.

Introduction

Pancreatic resections, especially pancreaticoduodenectomy (PD), are known to be among the most complex abdominal surgeries. In experienced centre, the mortality from pancreatic surgeries has reduced significantly over the past few decades [1, 2]. However, morbidity, which mainly includes delayed gastric emptying, anastomotic leak (bile and pancreatic juice) and post-operative pancreatic fistula (POPF), is still high (20% to 40%) [3, 4].

Post-pancreatectomy hemorrhage (PPH) is a rare but potentially life-threatening complication with an estimated mortality rate of 20% to 50% [5, 6]. Early bleeding, which occurs in the immediate post-operative period (<24 hours), is usually related to surgical techniques. In contrast, delayed or late hemorrhage, which occurs after 24 hours of surgery, is due to a variety of reasons, the most important of which results from the formation of visceral artery pseudoaneurysms [7, 8]. Historically, emergency surgery was the first-line treatment to achieve complete hemostasis in cases of delayed PPH [9]. However, in the past decade, with the advancement in the techniques of interventional radiology (IR), treatment strategy has largely shifted from surgery to IR [9].

A few previous studies have described late hemorrhage due to the rupture of pseudoaneurysms [10, 11]. However, the treatment protocol, prognostic factors and long-term outcomes after interventional treatment are still not known clearly. With this background, we aimed to retrospectively analyze the clinical parameters, surgical and embolization details and the outcomes of treatment in patients presenting with delayed hemorrhage due to pseudoaneurysms after pancreatic surgery.

Methodology

Patients

All patients who underwent surgery for pancreatic diseases in the department of gastrointestinal surgery between January 2014 and June 2020 were evaluated retrospectively. The study was approved by the Institute Ethics Committee and informed consent was waived. Medical records of all these consecutive patients were reviewed from a prospectively maintained database. All patients who presented with late bleeding after surgery and underwent digital subtraction angiography (DSA) were included in the present study. The demographic characteristics, type of surgery, clinical details related to delayed hemorrhage, including sentinel bleed rate, other associated complications (postoperative pancreatic fistula, bile leak), interventions performed for the delayed PPH and outcomes after treatment (complications, recurrence, mortality), were analyzed.

Definitions

Post-pancreatectomy hemorrhage (PPH)

PPH was defined according to the International Study Group of Pancreatic Surgery (ISGPS) criteria [12]. It included two categories: early hemorrhage, occurring in the first 24 hours post-operatively and late or delayed hemorrhage, occurring more than 24 hours after surgery.

Sentinel bleed

Any evidence of bleeding in the surgical drains or gastrointestinal tract six to 24 hours before a massive hemorrhage was termed sentinel bleeding.

Postoperative pancreatic fistula (POPF)

POPF was graded according to the International Study Group on Pancreatic Surgery (ISGPS) criteria (biochemical leak, grade B and grade C) [13].

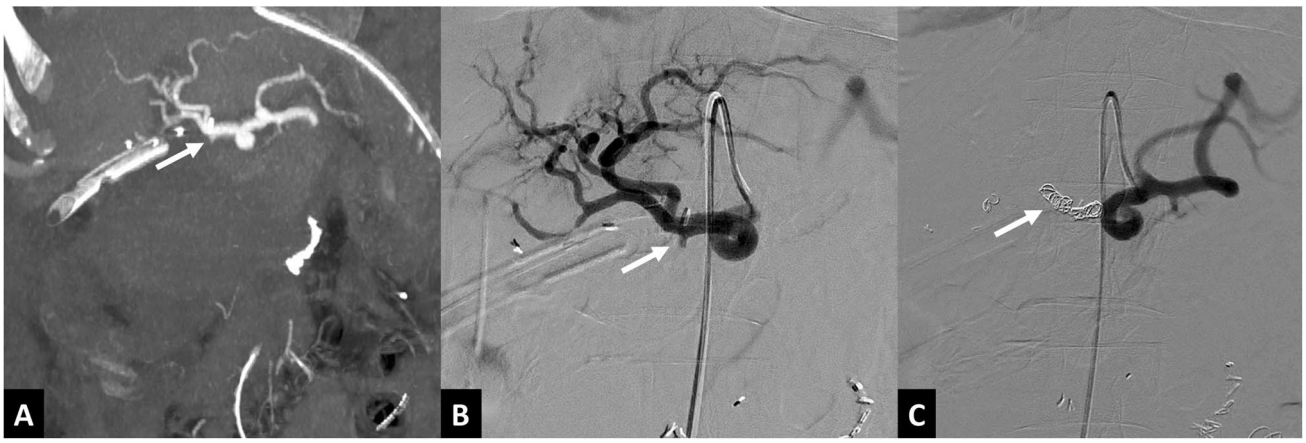

Fig. 1 Seventy-year-old male who underwent pancreatoduodenectomy for periampullary carcinoma, came with bleeding from drainage catheter three days after the surgery. **A** Coronal computed tomography (CT) angiography image shows a small pseudoaneurysm at the level of gastroduodenal artery stump (arrow). **B** Digital subtraction angiography of common hepatic artery shows the pseudoaneurysm (arrow). **C** Digital subtraction angiography image after embolization of the hepatic artery trunk with coils (arrow) shows exclusion of the pseudoaneurysm

Computed tomography angiography

All patients who presented with delayed PPH were initially resuscitated. Once they were hemodynamically stable, they underwent computed tomography (CT) angiography prior to DSA. CT angiography was performed on a 40-slice multidetector CT scan (Somatom Sensation, Siemens, Erlangen, Germany) or 128 slice dual-source CT (Definition Flash, Siemens, Erlangen Germany) after an injection of iodinated contrast agent intravenously. The scans of the abdomen were performed in the arterial and venous phases. The images of both phases were evaluated in multiple planes to identify any source of bleeding. Arterial source of bleeding was suggested, when there was active contrast extravasation, pseudoaneurysm or a spastic artery surrounding a hematoma. Patients who were found to have an arterial source of bleeding were shifted to interventional suite for embolization.

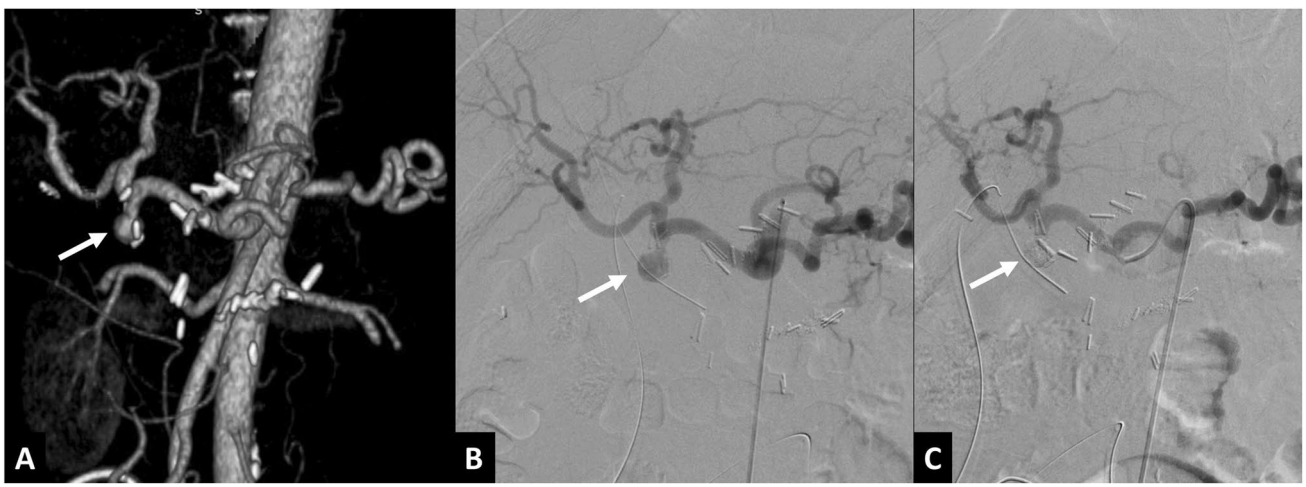

Fig. 2 Fifty-nine-year-old male who underwent pancreatoduodenectomy for pancreatic carcinoma, came with hematemesis and bleeding from drainage catheter six days after the surgery. **A** Volume rendered computed tomography (CT) angiography image shows a pseudoaneurysm arising from the gastroduodenal artery stump (arrow). **B** Digital subtraction angiography of celiac trunk shows the pseudoaneurysm (arrow). **C** Digital subtraction angiography after selective embolization of the pseudoaneurysm with n-butyl cyanoacrylate glue – ethiodized oil mixture (arrow) shows exclusion of the pseudoaneurysm

Angiographic embolization

DSA was performed in patients who showed an arterial source of bleeding on CT angiography, continued bleeding despite normal CT angiography or were hemodynamically unstable. Transfemoral route was used for the procedure.

When the source was identified on CT angiography, that particular territorial artery (celiac or superior mesenteric) was catheterized initially followed by superselective catheterization of the bleeding artery using a 2.7F microcatheter (Progreat, Terumo, Japan). In the absence of an identified source, angiographies of celiac, hepatic, gastroduodenal, left gastric, splenic and superior mesenteric arteries were performed sequentially to identify the source. Once the souce was identified, microcatheter was used for superselective catheterization.

Once the bleeding artery was catheterized, the microcatheter was passed distal to the site of bleeding or the pseudoaneurysm and embolization was performed using micro-coils and the standard "sandwich" technique (Fig. 1) [14]. When the microcatheter could not be passed distally due to either tortuosity or small caliber or when the partent artery was large, either proximal embolization or superselective embolization was performed with coils, n-butyl cyanoacrylate (NBCA) glue or a combination of coils and glue (Fig. 2). After embolization, final angiography was performed to confirm the exclusion of the bleeding point from the circulation.

Patient outcomes and evaluation

The severity and the nature of the bleed and the success of the embolization procedure performed were evaluated. The technical success of embolization was defined as complete occlusion of the bleeding source at the end of the procedure and clinical success as the absence of further hemorrhage from the same bleeding site after embolization in the next 30 days. Any adverse events related to angiography or embolization were recorded and graded according to the Society of Interventional Radiology Clinical Practice Guidelines [15]. In case of rebleeding, CT angiography or DSA or both were performed and whenever necessary the lesion was embolized. When embolization failed to achieve hemostasis or when vital signs were not stable for embolization, relaparotomy was performed. Mortality was defined as death occurring during the hospital stay or within 90 days of the index surgery. All patients were followed up clinically after discharge and the long-term clinical outcome was assessed.

The patients developing late PPH were grouped into those with and without pseudoaneurysms. The patient demographics, type of surgery and other surgical complications, clinical presentation and PPH-related parameters, recurrence and mortality were compared between the two groups.

Statistical analysis

The data was compiled in a Microsoft Excel worksheet and statistical analysis was done using Software Package for Social Sciences (SPSS) version 26.0 (SPSS Inc., IBM, Chicago, USA). The categorical variables were expressed as numbers and percentage. Normally distributed continuous variables were expressed as mean ± standard deviation, while skewed continuous variables were expressed as median and range. The categorical variables were compared using the Chi-square test or Fisher's exact test as indicated. The normally distributed continuous variables were compared using Student '*t*'-test or paired '*t*'-test as

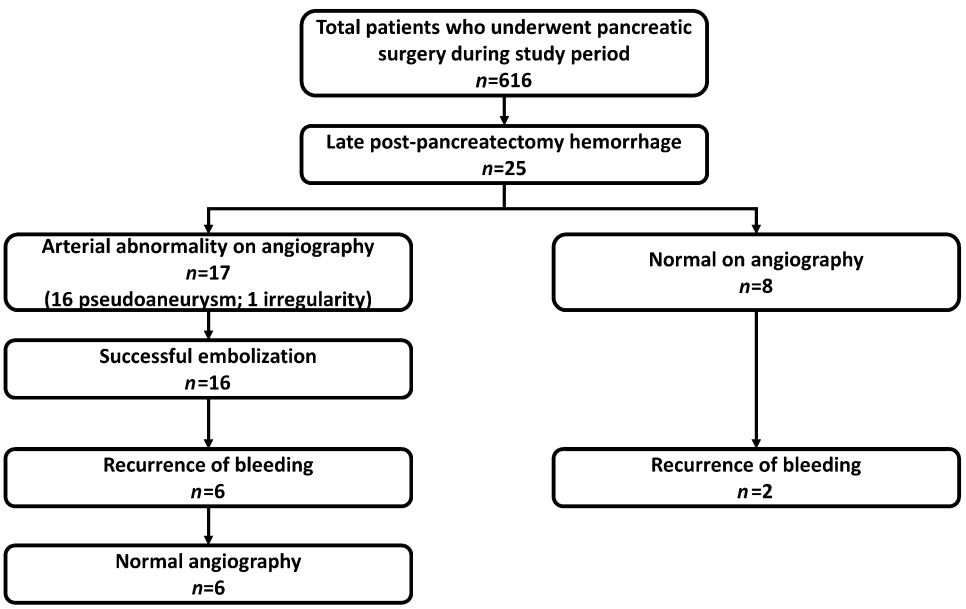

Fig. 3 Flowchart of the study

Table 1 Details of pancreatic surgeries

Surgery	No ($n=616$)	Pseudoaneurysm: $n=16$ (2.59%)
Pancreaticoduodenectomy	326	7 (2.1%)
Necrosectomy for acute pancreatitis	97	3 (3%)
Surgeries for chronic pancreatitis (Frey's procedure or lateral pancreatojejunostomy)	63	2 (3.1%)
DP and DPS	52	1 (1.9%)
Cystogastrostomy	29	1 (3.4%)
Enucleation	22	1 (4.5%)
Others (TP, CP, DPPHR, Cavitojejunostomy, biopsy, etc.)	27	1 (3.7%)

DP distal pancreatectomy, *DPS* distal pancreatosplenectomy, *TP* total pancreatectomy, *CP* central pancreatectomy, *DPPHR* duodenum-preserving pancreatic head resection

indicated. Skewed continuous variables were compared using non-parametric tests. A p-value of <0.05 was considered statistically significant.

Results

Total 616 patients underwent pancreatic surgery during the study period (Fig. 3). The types of pancreatic surgeries performed during this period are listed in Table 1.

Table 2 Baseline characteristics of patients who underwent angiography for late hemorrhage

Age (mean ± SD)	48 ± 16 years
Sex (male:female)	19:6
DSA for late bleed, *n*	25 patients
Bleed, *n* (%)	
Intraluminal only	7 (28%)
Extraluminal only	11 (44%)
Both	7 (28%)
Patients with pseudoaneurysm on DSA, *n* (%)	16 (2.59%)
Hb fall in g/dL (mean ± SD)	2.20 ± 1.04
Interval between surgery and bleed (mean ± SD)	16.25 ± 8.3 days
Sentinel bleed, *n* (%)	9 (36%)
Pancreaticoduodenectomy	6 (6/9; 66.6%)
Surgery for chronic pancreatitis	1 (1/9; 11.1%)
Distal pancreaticosplenectomy	1 (1/9; 11.1%)
Cystogastrostomy	1 (1/9; 11.1%)
Associated complications, *n* (%)	
POPF-CR	18 (72%)
Bile leak	13 (52%)
Surgery for bleeding after DSA, *n* (%)	5 (20%)
Rebleed, *n* (%)	6 (24%)
Mortality (in hospital and 90 days), *n* (%)	12 (48%)

DSA digital subtraction angiography, *SD* standard deviation, *Hb* hemoglobin, *POPF-CR* clinically relevant postoperative pancreatic fistula

Pancreaticoduodenectomy ($n=326$; 52.9%) was the most common pancreatic surgery performed followed by necrosectomy ($n=97$; 15.7%).

Total 25 patients (4.1%) (mean age: 48 years; 19 males; 6 females) developed late PPH following surgery and subsequently underwent CT angiography and DSA. The baseline characteristics and clinical parameters of these patients are presented in Table 2. Although extraluminal bleed ($n=11$; 44%) was more commonly seen, a fair share of patients ($n=7$; 28%) had both extraluminal and intraluminal bleed. The mean time interval between surgery and bleed was 16.25 ± 8.3 days with a mean hemoglobin fall of 2.2 ± 1.04 g/dL at the time of bleed. Sentinel bleed rate was 36% ($n=9$) and was more common in patients who underwent pancreaticoduodenectomy ($n=6$; 66.6%).

All embolization procedures were performed by two interventional radiologists with 12 and 25-year experience in gastrointestinal interventions. Arterial pseudoaneurysm (PSA) was identified in 16 out of 25 patients (64%) on DSA. One patient (1/25; 4%) had irregular outline of the artery. CT angiography detected the PSA in 14 patients (87.5%) and in two remaining patients PSA was identified on subsequent DSA performed for persistent bleeding. The source of PSA are listed in Table 3.

Table 3 Arterial source of pseudoaneurysm on angiography

Celiac artery territory: $n=11$ (68.7%)	
Gastroduodenal artery	6 (37.5%)
Common hepatic artery	1 (6.2%)
Cystic artery	1 (6.2%)
Splenic artery	1 (6.2%)
Right gastroepiploic artery	1 (6.2%)
Superior pancreaticoduodenal artery	1 (6.2%)
SMA territory: $n=5$ (31.2%)	
Inferior pancreaticoduodenal artery	4 (25%)
Middle colic artery	1 (6.2%)

SMA superior mesenteric artery

Gastroduodenal artery (GDA) was the most common site ($n=6$; 37.5%) followed by inferior pancreaticoduodenal artery (IPDA; $n=4$). In one patient, there was irregularity of the GDA and was suspected to be the source of bleeding. We used sandwich technique for embolization in eight patients by coils. In the remaining patients, proximal embolization with glue ($n=5$) and gelfoam ($n=3$) was performed as there was no distal access. Embolization procedure was successful in 16 of the 17 patients with a technical success rate of 94.1%. The embolic agents used were micro-coils ($n=7$), glue ($n=5$), gelfoam ($n=3$) and coils and glue ($n=1$). In one patient, where the PSA was arising from the proximal segment of middle colic artery, embolization was not performed as the artery could not be catheterized due to acute angulation. There were no procedure-related complications in any of the embolized patients.

No source of bleed was identified in the remaining eight patients (32%). In four of these patients, bleeding resolved spontaneously. In the remaining four patients, surgery was performed after a normal DSA for hemostasis. The source of bleed was the main portal vein in one patient, whereas in the remaining three patients, no definite source could be identified and the surgical site was packed for hemostasis.

Recurrence of bleed was seen in six patients (24%) after a median duration of 17 days (7–47 days) after initial embolization. Five of these patients had POPF and three patients had bile leak. CT angiography and DSA were performed in all and they did not reveal any pseudoaneurysm or source of bleed in these patients. Bleed was self-limited in five patients and relaparotomy with packing was required in one patient. The clinical success rate of the embolization procedures was 100%, as there was no rebleed from the embolized vessels or in their territory.

Clinically relevant POPF (72%) and bile leak (52%) were the most commonly associated complications in patients with late PPH. The comparison between patients with PSA and without PSA on DSA is shown in Table 4. Patients with PSA had significant hemoglobin drop (2.5 g/dL vs. 1.5 g/dL, $p=0.01$), more often had sentinel bleed (50% vs. 11.1%, $p=0.05$) and did not require surgery for bleeding (0% vs. 44.4%, $p=0.02$). The rest of the parameters, including the nature of bleed, associated complications, rebleed rates and mortality, were similar between both groups.

The total in-hospital and 90-day mortality in this whole cohort was 48% ($n=12$), but none of them was due to bleeding as the direct cause for mortality. Sepsis, because of associated complications, was the cause for mortality in all. Five patients (5/6; 83.3%) who had recurrent bleeding died compared to seven patients (7/19; 36.8%) who did not develop rebleed. Finally, 13 patients (13/25; 52%) were discharged and followed up for a median period of 26.5 months (range: 1–36 months). Three of these patients (two in the embolized group) died during follow-up due to metastatic disease. The remaining 11 patients (six of whom were embolized) were doing well without any clinical symptoms at the time of the last follow-up.

Discussion

Post-pancreatectomy hemorrhage, albeit a relatively rare complication, has very high mortality rate [16]. The differentiation between early and late PPH is essential as both have varied etiologies, management strategies and prognosis. Late PPH is frequently associated with other complications such as POPF

Table 4 Comparison between patients with and without pseudoaneurysm on angiography

Parameters	Pseudoaneurysm on DSA ($n=16$)	No pseudoaneurysm on DSA ($n=9$)	p-value
Age (mean ± SD), years	51 ± 15	43 ± 18	0.23
Pancreaticoduodenectomy (n)	7	5	0.66
Interval between surgery and bleed (mean ± SD), days	16.75 ± 7.7	15.25 ± 9.8	0.68
Type of bleed (n)			
Intraluminal	5	2	
Extraluminal	7	4	0.85
Both	4	3	
Hb fall (g/dL) (mean ± SD)	2.5 ± 0.99	1.55 ± 0.81	**0.01**
Bile leak, n (%)	8 (50%)	5/8 (62.5%)	0.56
POPF-CR, n (%)	11 (68.7%)	7/8 (87.5%)	0.47
Surgery for bleeding, n (%)	0 (0%)	4 (44.4%)	**0.02**
Sentinel bleed, n (%)	8 (50%)	1 (11.1%)	**0.05**
Rebleed, n (%)	4 (25%)	2 (22.2%)	0.87
Mortality, n (%)	8 (50%)	4 (44.4%)	0.79

DSA digital subtraction angiography, *SD* standard deviation, *Hb* hemoglobin, *POPF-CR* clinically relevant postoperative pancreatic fistula (p-values in bold indicate significant at ≤ 0.05)

and has much higher mortality rates (20% to 50%) [5, 17]. Clinically relevant POPF was the most common complication (72%) associated with late PPH in our study. A few other studies have also confirmed this association with clinically relevant POPF being reported in upto 80% cases of late PPH [18–20]. A meta-analysis also showed an association of late PPH with POPF in 65% of patients [17]. The leak of pancreatic and bile juices from the anastomotic site and associated infection and intra-abdominal abscess formation leads to erosion of vessels resulting in the development of pseudoaneurysms [16]. It has been reported that clinically relevant POPF is an independent risk factor for the development of pseudoaneurysm related bleed and increases the mortality by 17-fold [21].

Angiographic embolization is an important armamentarium and, due to its less invasive nature, has become the preferred treatment in the management of PPH. DSA, being the gold standard, can identify PSA missed on CT angiography, as was shown in our study. The technical and clinical success rates following endovascular interventions in our study were 94.1% and 100%, respectively, with a rebleed rate of 24%. Various studies have shown that the technical success of endovascular intervention for late PPH ranges between 82% and 100% and reported rebleed rates between 7% and 30% [22–25]. Technically, the recurrent bleed in our study was not truly due to failed embolization as there was no bleeding from the embolized vessel. Also, the median time to rebleed was 17 days, which reiterates that the associated complications, including POPF and bile leak, were the possible causes. Furthermore, the mortality rate in patients with rebleed was much higher (83.3%) reflecting the severity of associated complications.

In our study, comparision between groups with and without PSA showed that the probability of finding a PSA is higher when there is sentinel bleed and higher mean hemoglobin fall. Sentinel bleed preceding major hemorrhage was seen in 50% of patients with PSA. In the existing literature, the incidence of sentinel bleed preceding a severe PPH is reported to be between 50% and 80% [25–28]. Thus, sentinel bleed associated with a fall in hemoglobin should warrant an immediate CT angiography and, if necessary, DSA and embolization. Inspite of the high technical (94.1%) and clinical (100%) success rate of embolization, the mortality rate among patients with late PPH in our study was high (48%) indicating that a successful hemostasis alone did not directly translate into improved survival in patients with late PPH. Bleeding was not a cause for death in any of our patients and associated complications such as POPF and bile leak leading to sepsis and multi-organ dysfunction were responsible for high mortality [29]. There are no studies with long-term outcome of patients with late PPH following successful embolization in the existing literature. In our study, the long-term outcome of these patients was undeterred from late bleed once they were discharged home.

At our institute, CT angiography is the first modality performed for the diagnosis of the cause for post-operative bleeding. CT angiography helps in identifying the cause for the hemorrhage, guiding further management, providing a roadmap for subsequent DSA and reducing the time and radiation of the DSA procedure [30]. Although some propose performing a DSA directly, we believe that it is invasive and does not identify non-arterial sources of bleeding [31]. However, in a patient who is hemodynamically unstable, DSA may be performed as an initial modality with the aim of simultaneous embolization.

GDA stump is the most common site of PSA following pancreatic surgeries and is difficult to treat [32, 33]. Selective embolization of the GDA stump will preserve the hepatic arterial flow, but this is technically challenging due to the risk of reflux of embolic agents, non-target embolization and rebleed [14]. A successful selective embolization depends on the length of the GDA stump and the morphology of the PSA [22, 34, 35]. In a study by Hur et al., there was 100% rate of rebleed after selective embolization of the GDA stump [22]. Placement of stent grafts will also preserve hepatic arterial flow, but are associated with different sets of problems such as technical difficulty because of angulation, higher cost, endoleaks and thrombosis [36, 37]. A recent study comparing hepatic artery sacrifice, superselective embolization and stent graft placement for delayed PPH found that hepatic artery sacrifice method is more effective than superselective embolization and stent graft is a reasonable alternative [38]. In our study, GDA stump PSA was found in six patients, three of whom were embolized superselectively and in the remaining three, hepatic artery was sacrificed by coil embolization. All six embolizations were clinically successful.

There were a few limitations in this study. First, the study design was retrospective. Data accrued were inhomogeneous with respect to the disease, surgeries performed and post-operative complications. Second, the sample size was small. Although the incidence of late PPH was similar to that found in literature, the sample may not be representative. Third, a multivariate analysis was not done due to the small sample size.

In conclusion, late PPH is a severe complication significantly associated with complications such as POPF and bile leak and with high mortality rate. The most common cause is an arterial PSA, which can be managed effectively with endovascular intervention with a very high success rate. Since a successful embolization of the PSA does not determine patient survival, meticulous attention to prevent surgical complications and provide intensive treatments before and after embolization may be necessary to improve clinical outcomes.

Declarations

Conflicts of interest JK, RP, ANS, NRD, SP, DNS, PS and MSM declare no competing interests.

Ethics statement The study was performed conforming to the Helsinki Declaration of 1975, as revised in 2000 and 2008 concerning human and animal rights, and the authors followed the policy concerning informed consent as shown on Springer.com.

Ethics approval The study is approved by the Institute Ethics Committee.

Informed consent The Institute Ethics Committee waived the informed consent for this retrospective study.

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