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Bleeding pancreatic pseudoaneurysms: management by angioembolization combined with therapeutic endoscopy

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Abstract
Background Bleeding pancreatic pseudocysts (PPCs) are a rare but lethal complication of pancreatitis. Transcatheter arterial embolization (TAE) is the first-line treatment of acute hemorrhage, but consensus on the definitive management of bleeding PPCs is lacking. The aim of this study was to evaluate the safety and efficacy of the combination of TAE and therapeutic endoscopy in the treatment of bleeding PPCs.
Methods Patients with acute or chronic pancreatitis treated for bleeding PPCs in Helsinki University Hospital during 2004–2014 comprised the study group. Inpatients with acute necrotizing pancreatitis were excluded. Patients underwent TAE as the primary treatment to control the bleeding. Therapeutic endoscopy performed on an outpatient visit after TAE allowed the definitive treatment of PPCs.
Results A total of 58 patients underwent TAE. Re-bleeding rate (<30 days) was 15.5 %, necessitating re-embolization on seven and surgical intervention on two patients. Overall, TAE success rate was 96.6 %. Mortality rate (<30 days) was 3.4 %. Of the 58, 47 patients were followed up for their PPCs in our unit. PPCs resolved spontaneously in 13 (27.1 %). The remaining 34 had an endoscopic treatment attempt with endoscopic draining performed on 32 and unsuccessful cannulation on two (5.9 %). Of the 32 patients with initially successful endoscopy, 7 (21.9 %) needed an additional drainage procedure (six non-surgical and one surgical). Overall success rate of non-surgical management was 91.5 %. Post-endoscopy mortality rate (<30 days) was 2.9 %. Our follow-up continued for 15 (1–75) months. By the time of data retrieval, 35 of 58 patients had died with alcohol liver disease being the most common cause of death. Five-year survival estimate was 63 %.
Conclusions Bleeding pancreatic pseudoaneurysms require non-surgical management. We need more data on the optimal timing of therapeutic endoscopy and on the role of empirical embolizations.

Keywords Pancreatitis · Pseudoaneurysm · Pseudocyst · Arterial embolization · Endoscopy

Approximately 5–40 % of patients with acute (AP) and chronic pancreatitis (CP) experience the formation of pancreatic pseudocysts (PPCs) [1]. Chronic inflammation and digesting pancreatic enzymes can produce aneurysms in nearby visceral arteries. Such visceral artery aneurysms (VAAs) may rupture into the PPCs, transforming them into pancreatic pseudoaneurysms (PPAs). Spontaneous PPA hemorrhage is a rare but lethal complication of pancreatitis; it occurs in 1–5 % of patients [2–4], and, if left untreated, has a mortality of up to 90 % [5].

The recommended first-line treatment for bleeding PPAs, with success rates of 67–97 % and mortality rates of 4–19 %, is transcatheter arterial embolization (TAE) [4, 6–8]. The traditional surgical treatment with vessel ligation or pancreatic resection leads to higher morbidity and mortality in patients who are often hemodynamically compromised. Thus, surgery is indicated only if TAE fails or is not feasible [5, 9].

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With symptomatic or complicated PPCs, a consensus exists as to the need for their active treatment [10–12]. The modern treatment of choice is therapeutic endoscopy with transpapillary or transmural stenting. Endoscopy is more cost-effective (associated with shorter hospital stays) than traditional surgical treatment and comparable to surgery in efficacy [13, 14]. After embolization of bleeding PPAs, however, consensus on the preferred treatment approach is still lacking [5].

Even if TAE has an established role in the management of PPA hemorrhage, as has therapeutic endoscopy in the treatment of complicated PPCs, data on the efficacy of the combination of these methods as a definitive treatment of bleeding PPAs are limited; only three publications, mere case reports, address non-surgical treatment for this clinical entity [15–17]. Important questions such as optimal timing of therapeutic endoscopy after TAE remain. Long-term treatment results are also lacking.

According to our hypothesis, the non-surgical management of bleeding PPAs with a combination of interventional radiology and therapeutic endoscopy is safe and efficient. The aim of this study is to evaluate the clinical outcomes of this multidisciplinary two-step approach.

Patients and methods

Patient selection and data sources

Our study group comprised patients treated for bleeding PPAs in Helsinki University Hospital (HUH) during 2004–2014. Patients who had a bleeding VAA or PPA as a consequence of AP or CP, and who received TAE as their primary treatment, were included. To establish a homogenous study group, acute necrotizing pancreatitis, no underlying pancreatitis, or surgical treatment as primary treatment resulted in exclusion. To identify the patients, we reviewed HUH surgical interventions database and interventional radiology unit database. ICD-10 codes K85.xx–K86.xx for AP and CP and their complications were used in database search. We found 74 patients altogether, 58 of these meeting the inclusion criteria for the analysis of the safety and efficacy of TAE (Fig. 1). Of the group of 58 patients, 55 had a PPC. Five of these were referred to our hospital only for angiography and TAE, the final treatment of PPC taking place elsewhere. Three patients did not receive endoscopic treatment for their PPCs: Two died soon after TAE, and one received percutaneous draining for splenic collection. This leaves 47 patients with PPCs suitable for the analysis of the safety and efficacy of the non-operative management of PPCs after TAE (Fig. 2).

CT and angiography findings confirmed the presence of VAA hemorrhage or PPA. A review of patient medical history with computed tomography (CT) and endoscopic retrograde cholangiopancreatography (ERCP) findings, and fecal elastase level, when measured, allowed the diagnosis of AP or CP. When reviewing comorbidities, we coded the patient to have alcoholism or alcohol-induced pancreatitis only when it was explicit from the patient history and clinical findings. Hospital medical records provided details on patients at baseline, admission time, imaging methods and findings, initial therapy and further procedures, as well as the success and complication rate of therapeutic interventions (<30 days, total). ERCP complications defined by Cotton et al. [18] and TAE complications defined by Barge et al. [19] were recorded. Collected data include also time and cause of death.

Setup and technique for transcatheter arterial embolizations

HUH receives 24/7 services from interventional radiologists that performed the intravascular treatment on VAAs and PPAs. Depending on patient's hemodynamics, the embolization procedure took place in the unit of interventional radiology or in a hybrid theater designed for combined intravascular and open procedures, allowing general anesthesia with invasive monitoring and conversion to emergency surgery if necessary. Postoperative monitoring of embolized patients continued at a surgical ward, in a high-dependency unit, or in an intensive care unit. Rebleeding necessitating repeated angiography or surgery within 30 days of embolization indicated clinical failure.

Our routine protocol in performing TAE on bleeding PPAs and VAAs begins by gaining arterial access through the common femoral artery. Gastroduodenal artery, splenic artery and superior mesenteric artery are selectively catheterized and visualized by angiography (Fig. 3). When detecting PPA, VAA or extravasation of contrast agent as a sign of acute bleeding, the damaged arterial segment is embolized proximally and distally to the bleeding site. The routine embolization method is coiling with microcatheter and microcoils. If the patient has a history with hemorrhage but no bleeding site detectable in angiography, the interventional radiologist and surgeon evaluate each case individually. If a consensus on the arterial segment most likely causing the bleeding exists, empirical embolization follows.

Setup and technique for endoscopic management of pseudocysts

CT scan or ultrasound done on a follow-up visit, allowed determination of any remaining PPCs. The definitive treatment of such PPCs took place in the unit of therapeutic endoscopy of HUH, where the number of ERCP procedures totals 1300 per year, including the management of approximately 60 PPCs annually. Gastrointestinal surgeons with experience in therapeutic endoscopy performed the

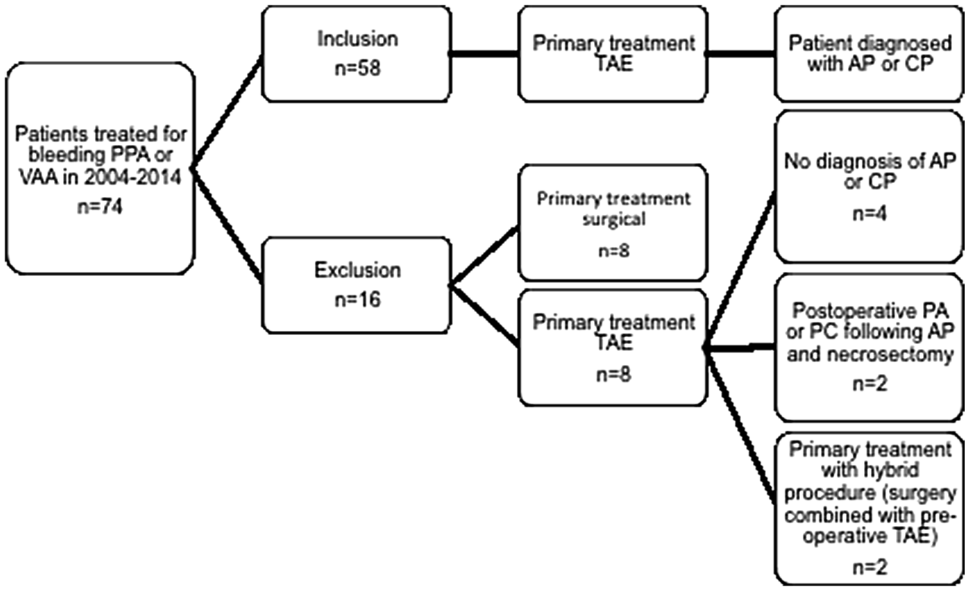

Fig. 1 Inclusion and exclusion protocol of the study on the safety and efficacy of transcatheter arterial embolizations (TAE) in the treatment of bleeding pancreatic pseudoaneurysms (PPAs) and visceral artery aneurysms (VAAs) in acute (AP) and chronic pancreatitis (CP)

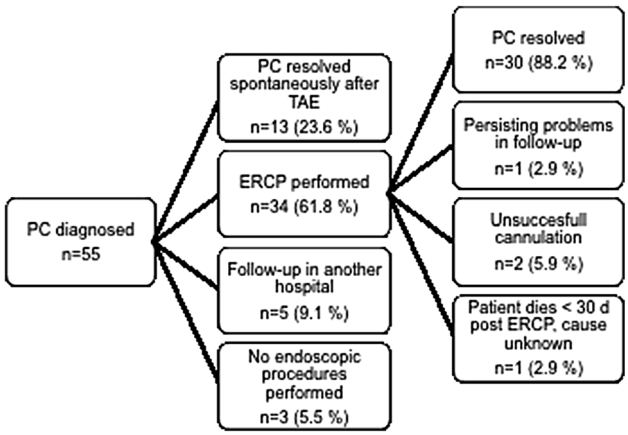

Fig. 2 Follow-up and treatment of pancreatic pseudocysts after transcatheter arterial embolization

procedures with pancreatic duct stenting, pseudocystogastrostomy and pseudocystoduodenostomy being the methods used. Biliary duct stenting was necessary if PPC caused biliary obstruction. Post-endoscopy follow-up included CT-imaging. A persisting or complicated PPC necessitating surgery indicated treatment failure.

Endoscopic treatment of PPCs took place a minimum of 2 weeks following TAE in order to avoid infection and re-bleeding complications. We exploited transpapillary route, if the PPC was not in immediate contact with gastric or duodenal wall. Pancreatic duct strictures necessitated pancreatic sphincterotomy followed by dilatation over guidewire and insertion of 1–4 (7–10 Fr) pancreatic stents. Aim was to at least pass the stricture with stent and, if possible, bridge communication between pancreatic duct and PPC. Follow-up included a CT scan scheduled 2 months later. Stents remained in place as long as the PPC was detectable in a CT scan. Further follow-up comprised control imaging followed by exchange or removal of stents in 6–12 months.

We chose transmural route to drain a PPC, when CT scan showed a PPC in immediate contact with gastric or duodenal wall. Duodenoscopy enabled the penetration of PPC wall with a Zimmon needle knife papillotome (Wilson Cook Medical, Winston-Salem, NC, USA) after visualizing the bulging site. We use endoscopic ultrasound (EUS) in transmural drainage only when the PPC is not bulging intraluminally [20]. In this study, we used EUS with one patient. Routine sampling of pseudocyst contents produced material for bacterial culture. After introducing a guidewire (Jagwire Super Stiff; Boston Scientific Microvasive, Natick, MA, USA) and dilatation of the tract with an 8-mm biliary balloon (MaxForce, Boston Scientific Microvasive), the PPC received one or more Zimmon double-pigtail (10 Fr) stents with a distance of 2 cm between the loops (Wilson Cook Medical). If follow-up CT scan in 2 months showed resolution of PPC, pseudocystoduodenostomies were removed usually 6 months after the procedure. Pseudocystogastrostomies were left in situ indefinitely as has been our standard over the years without any problems [21]. The optimal timing of transmural stent removal is unclear, and some studies even show fewer PPC recurrences with delayed stent removal [22, 23].

Statistical analysis

IBM SPSS Statistic 22 was used for statistical analysis. Continuous variables are expressed with median (range)

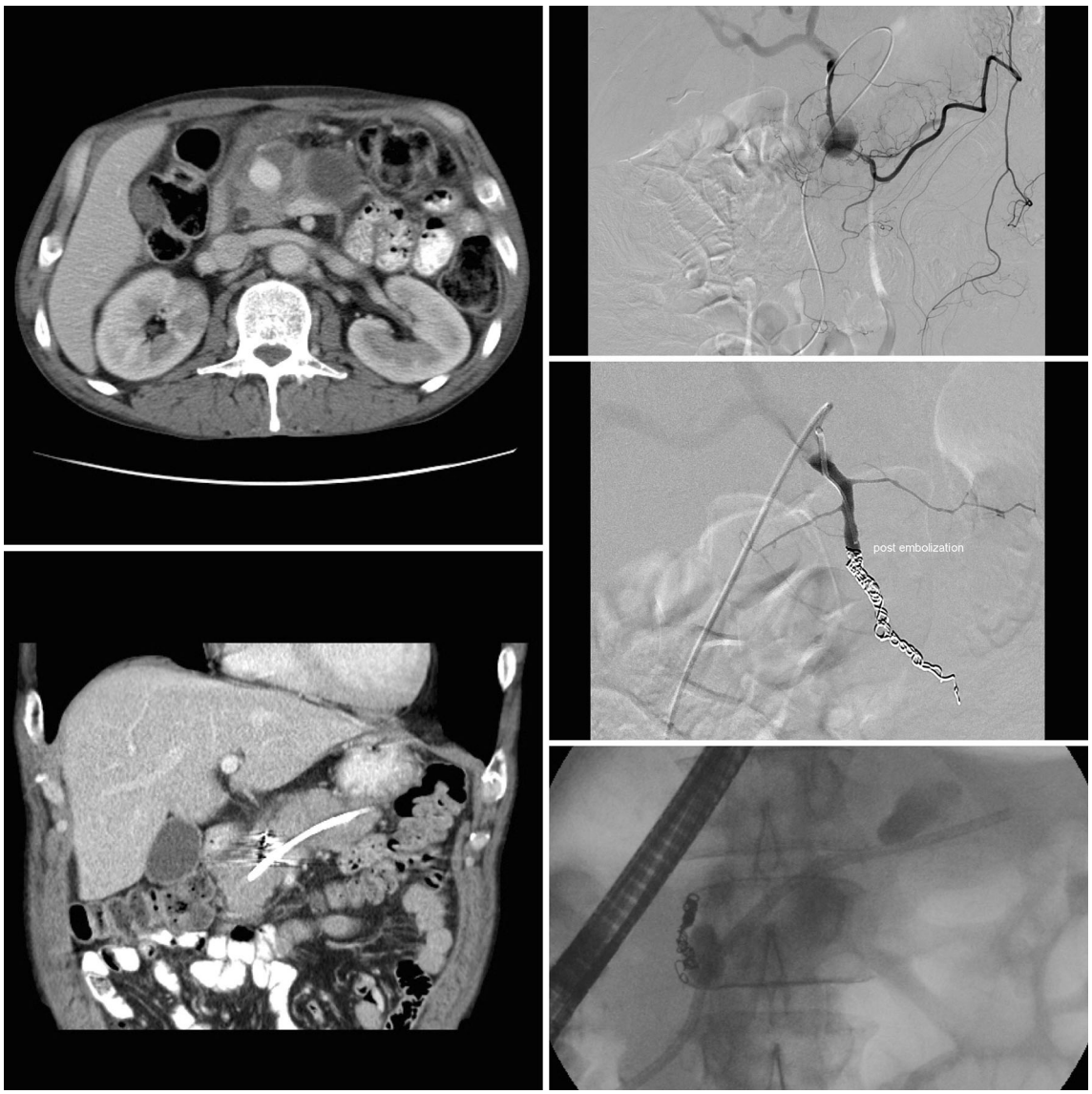

Fig. 3 A 52-year old man presented with melena. Gastroscopy was negative. *Top left* Computed tomography (CT) showed a 3.4-cm pancreatic pseudoaneurysm in the pancreatic head. *Top right* Digital subtraction angiography (DSA) detected a pseudoaneurysm of gastroduodenal artery (GDA). *Right middle* Control DSA after coiling of GDA showed no more filling of the pseudoaneurysm. *Bottom right* Endoscopic retrograde cholangiopancreatography (ERCP) with pancreatic duct stenting was scheduled 1 month after angioembolization. *Bottom left* Control CT 2 months after pancreatic duct stenting showed the resolution of pseudocysts

and categorical variables as percentages. Mann–Whitney *U* test was utilized to compare the distributions of continuous variables and Chi-square test or Fisher's exact test to compare categorical data between groups. Kaplan–Meier analysis enabled the estimation of survival.

Ethical approval

The institutional ethical committee approval to conduct retrospective research using patient files was applicable in our study.

Results

Patients' characteristics

All patients had their initial evaluations at the emergency department of HUH (Tables 1, 2). One of them underwent an exploratory laparotomy on the day of TAE in another hospital with no bleeding site found. Of the 58 patients, 22 (37.9 %) presented with hematemesis or melena. Gastroscopy was done on 16 patients, five of these showing bleeding from papilla. All but one patient received an

emergency CT scan (Table 3). If it showed a PPA or VAA suspicious for bleeding, angiography was necessary. One patient underwent elective ERCP for a PPC detected earlier, when bleeding from papilla revealed hemorrhage from PPA necessitating TAE. Of the 58 patients, 6 (10.3 %) had a CT scan showing only PPC or VAA but no signs of active bleeding. Clinical presentation and other findings directed the decision to proceed to angiography with these patients: Three had gastrointestinal bleeding. One had persistent anemia and episodes of upper of abdominal pain. One had upper abdominal pain only. A patient described earlier had an elective ERCP for PPC that revealed bleeding from papilla necessitating embolization.

Table 1 Patient baseline characteristics

	$n = 58$
Sex [*n* (%)]	
Male	48 (82.8)
Female	10 (17.2)
Age (years)	55 (26–73)[a]
Comorbidity [*n* (%)]	
Alcoholism	39 (67.2)
Cardiovascular disease	18 (31.0)
Diabetes mellitus	9 (15.5)
Clinical presentation [*n* (%)]	
CP	46 (79.3)
CP + PC + PA	39 (67.2)
CP + PC	4 (6.9)
CP + PA	3 (5.2)
AP	12 (20.7)
AP + PC + PA	7 (12.1)
AP + PC	5 (8.6)
Etiology of pancreatitis [*n* (%)]	
Alcohol	51 (87.9)
Idiopathic	7 (12.1)
Gallstones	0 (0)
History with documented episode of AP [*n* (%)]	
Yes	43 (74.1)
No	2 (3.4)
Unknown	13 (22.4)
Time elapsed after first episode of AP (months)	16 (0–155)[a]
Previous history with PC [*n* (%)]	
Yes	53 (91.4)
No	5 (8.6)
Previous procedure prior to embolization [*n* (%)]	
Yes	8 (13.8)
Pseudocystogastrostomy	3 (5.2)
Pseudocystoduodenostomy	1 (1.7)
ERCP + pancreatic stent + pseudocystogastrostomy	1 (1.7)
ERCP + pancreatic stent	1 (1.7)
Percutaneous drainage of PC	1 (1.7)
Explorative laparotomy	1 (1.7)
No	50 (86.2)

CP chronic pancreatitis, *PC* pseudocyst, *PA* pseudoaneurysm, *AP* acute pancreatitis, *ERCP* endoscopic retrograde cholangiopancreatography

[a] Median (range)

Table 2 Clinical findings on admission

	$n = 58$
Main complaints [*n* (%)]	
Abdominal pain	41 (70.7)
Melena	17 (29.3)
Hematemesis	12 (20.7)
Fever	6 (10.3)
Jaundice	2 (3.4)
None of the above	2 (3.4)
Main findings on clinical examination [*n* (%)]	
Abdominal tenderness	33 (56.9)
Melena	16 (27.6)
Hemodynamic instability	10 (17.2)
Palpable abdominal mass	6 (10.3)
Hematemesis	5 (8.6)
Body temperature > 38 °C	4 (6.8)
Jaundice	2 (3.4)
None of the above	7 (12.1)
Hemodynamic and clotting status	
Systolic blood pressure (mmHg)	135 (72–216)[a]
Systolic blood pressure < 100 mmHg [*n* (%)]	6 (10.3)
Heart rate (BPM)	88 (58–131)[a]
Heart rate > 100 BPM [*n* (%)]	13 (22.4)
Hemoglobin [B-Hb (g/l)]	100 (31–152)[a]
Hemoglobin < 100 g/l [*n* (%)]	28 (48.3)
Thrombocyte count, B-Trom, E9/l	303 (24–941)[a]
Thromboplastin time (TT%)	75 (14–513)[a]
Blood transfusions required prior to embolization, units of packed RBCs [*n* (%)]	
0	32 (55.2)
1–5	17 (29.3)
6–10	8 (13.8)
>10	1 (1.7)

BPM beats per minute, *RBC* red blood cell

[a] Median (range)

Transcatheter arterial embolization

All 58 patients received angiography and embolization with nine documented re-bleeds, indicating an initial angioembolization success rate of 84.5 % (Table 4). The most common bleeding sites were splenic artery explaining 30 (51.7 %) and gastroduodenal artery explaining 11 (19.0 %) of the bleeding episodes (Table 3). Of nine suspected re-bleeds, eight occurred within 30 days of initial embolization with the delay to reoperation being 9 days (0–30). One hepatic artery aneurysm had recanalized necessitating re-embolization 41 weeks after initial embolization.

Table 3 Imaging methods and findings on admission

	$n = 58$
Imaging modality [*n* (%)]	
CT without iv contrast (renal function)	1 (1.7)
Contrast-enhanced CT (dual phase)	19 (32.8)
Abdominal CT angiography (3 phases)	32 (55.2)
Aortic CT angiography (3 phases)	5 (8.6)
CT not done	1 (1.7)
VAA found in CT or angiography [*n* (%)]	
Yes	49 (84.5)
No	9 (15.5)
VAA diameter (cm)	2.1 (0.6–8.4)[a]
PC found in CT [*n* (%)]	
Yes	55 (94.8)
No	3 (5.2)
PC location in CT [*n* (%)]	$n = 55$
Head of pancreas	18 (32.7)
Head and body of pancreas	4 (7.3)
Body of pancreas	3 (5.5)
Body and tail of pancreas	13 (23.6)
Tail of pancreas	16 (29.1)
Whole pancreas	1 (1.8)
PC diameter in CT (cm)	5.9 (2.4–42)[a]
Hemorrhage of VAA/PC suspected in CT [*n* (%)]	$n = 57$
Yes	51 (89.5)
No	6 (10.5)
Active bleeding in CT angiography [*n* (%)]	$n = 37$
Yes	16 (43.2)
No	21 (56.8)
Bleeding site detected in angiography [*n* (%)]	
Yes	50 (86.2)
No	9 (15.5)
Suspected vessel in angiography [*n* (%)]	
Splenic artery	30 (51.7)
Gastroduodenal artery	11 (19.0)
Gastroepiploic artery	5 (8.6)
Superior mesenteric artery branches	4 (6.9)
Left gastric artery	4 (6.9)
Pancreaticoduodenal artery	2 (3.4)
Hepatic artery	2 (3.4)
Bleeding site (clinical presentation and imaging findings) [*n* (%)]	
Gastrointestinal tract	29 (50)
Limited in PC	21 (36.2)
Intra-abdominal	7 (12.1)
Retroperitoneal	1 (1.7)

CT computed tomography, *VAA* visceral artery aneurysm, *PC* pseudocyst

[a] Median (range)

Two of nine patients with suspected re-bleed underwent a repeated angiography with no hemorrhage detectable. Five underwent a successful re-embolization, showing that bleeding could be controlled with embolization in 96.6 %. Of nine patients with a clinical failure, two underwent a laparotomy. The first was performed after a negative angiography and empirical embolization due to suspected re-bleeding and pancreatic necrotic infection. After necrosectomy with hematoma evacuation from the omental bursa, still no bleeding site was detectable. The other

Table 4 Results: transcatheter arterial embolization

	$n = 58$
Embolization feasibility [*n* (%)]	58 (100)
Active bleeding embolized	50 (86.2)
Empirical embolization with no bleeding site detected	9 (15.5)
Embolization method [*n* (%)]	
Coiling	52 (89.7)
Stent	3 (5.2)
Particles	2 (3.4)
Plug	1 (1.7)
Clinical failure (re-bleeding < 30 days) [*n* (%)]	9 (15.5)
Re-intervention, angiography ($n = 7$) ± embolization ($n = 6$)	7
Re-intervention, surgery	2
Overall angioembolization success rate	56 (96.6)
Thirty-day morbidity (overall complication rate) [*n* (%)]	18 (31.0)
Splenic infarction	15 (25.7)
Minor infarction in follow-up CT	8
Large infarction or necrotic collection in follow-up CT	7
Drainage of splenic necrotic collection/abscess performed	4
Pseudocyst infection	1 (1.7)
Duodenal mucosal ischemia	1 (1.7)
Colon pseudo-obstruction and necrosis of cecum	1 (1.7)
Unknown (follow-up elsewhere)	4 (6.9)
Thirty-day mortality [*n* (%)]	2 (3.4)
Patient dies intraoperatively (bleeding complicated by DIC)	1
Patient dies 8 days postoperatively (COPD exacerbated by pneumonia, ARDS)	1
Hospital stay	
Length of stay at intensive observation unit or ICU ($n = 58$) (days)	0 (0–13)[a]
0 days [*n* (%)]	33 (56.9)
1–2 days	17 (29.3)
3–4 days	4 (6.9)
>5 days	4 (6.9)
Length of stay when discharged home ($n = 31$) (days)	3 (0–27)[a]
≤3 days [*n* (%)]	18 (58.1)
4–7 days	8 (25.8)
8–14 days	3 (9.7)
>14 days	2 (6.4)
Need for blood transfusions in total, units of packed RBCs ($n = 58$)	4 (0–28)[a]
0 units [*n* (%)]	18 (31)
1–5 units	20 (17.2)
6–10 units	13 (22.4)
>10 units	7 (12.1)

CT computed tomography, *DIC* disseminated intravascular coagulopathy, *COPD* chronic obstructive pulmonary disease, *ARDS* acute respiratory distress syndrome, *ICU* intensive care unit, *RBC* red blood cell

[a] Median (range)

laparotomy followed a series of therapeutic procedures: PPC in the pancreatic tail following acute pancreatitis received a pancreatic stent. PPC infection ensued, and a pseudocystogastrostomy was placed. PPC hemorrhage followed resulting in coiling of the splenic artery. Eventually, the infected PPA ruptured and re-bled intraperitoneally. A pancreatic tail resection with splenectomy was necessary. We compared patients with re-bleeding to patients with successful embolization and found no difference ($p > 0.05$) in their baseline characteristics (age, gender, hemodynamic status, clotting status) or CT findings (size and location of PPC or VAA).

Bleeding was undetectable in nine (15.5 %) patients' initial angiographies. All of these underwent an empirical embolization in the artery suspected as the bleeder based on CT findings. Three of such embolizations failed with the re-bleeds occurring 0, 8 and 18 days later. The first patient underwent an empirical embolization of gastroduodenal artery and pancreaticoduodenal artery. A repeated angiography showed active bleeding from superior mesenteric artery branches that were successfully coiled. The second patient underwent a repeated angiography for suspected re-bleeding after empirical coiling of splenic artery. Angiography detected no bleeding, but splenic artery was recoiled. No further bleeding occurred in these two patients. The third patient underwent a laparotomy that, after necrosectomy and omental bursa hematoma evacuation, led to no detection of bleeding site. The incidence of re-bleeds was not higher in patients who received empirical embolization ($p = 0.136$).

Discharge from the hospital was possible 3 (0–27) days after embolization. Need for blood transfusions during the hospital stay totaled 2 (0–18) units of packed red blood cells (Table 4).

The overall complication rate was 31 % (Table 4). Immediate procedure-related complications did not occur. A CT-confirmed splenic infarction following splenic artery embolization was the most common complication seen in 15 out of 30 (50 %) patients after TAE of splenic artery. In seven of these, a large infarction or a necrosis of the whole spleen was detectable. Splenic necrotic collections required draining in three patients. After coiling of splenic artery, one developed Ogilvie syndrome and necrosis of cecum necessitating laparotomy and right hemicolectomy. One patient complained post-embolization upper abdominal pain. Gastroscopy showed duodenal mucosal ischemic ulceration after embolization of gastroduodenal artery. Follow-up gastroscopy was normal a week later.

Endoscopic treatment of pancreatic pseudocysts

Follow-up imaging performed 8 (5–44) weeks after TAE showed spontaneous resolution of a PPC in 13 out of 47 patients (27.7 %) receiving treatment for their PPCs in our unit (Fig. 2). The remaining 34 underwent endoscopic treatment attempt. Five (14.7 %) received elective endoscopic treatment for their PPCs before the embolization. Pre-endoscopy CT of any of these patients did not detect the presence of VAA. Bleeding from PPC or VAA occurred 2 (0–20) weeks after endoscopy. Out of 34 patients, 29 (85.3 %) had an elective endoscopy 4 (2–45) weeks after TAE. One patient received pancreatic duct stent only 45 weeks later after a delayed re-bleeding episode. Cannulation of pancreatic duct was unsuccessful on two of 34 (5.9 %). Pulmonary carcinoma with a poor prognosis led to a decision to refrain from further procedures and follow-up with the first patient. The other suffered from alcoholism. Due to his poor general health, we scheduled follow-up without further interventions. First, the PPCs increased in number, but ultrasound 2 years later detected no PPCs.

Of the 32 patients, 7 (21.9 %) needed an additional procedure after the primary endoscopy due to a persisting PPC. Out of 24 patients with primary pancreatic duct stenting, 3 (12.5 %) received an additional drainage procedure (one transmural, one percutaneous and one surgical). Out of 8 patients with primary transmural drainage, 4 (50 %) received additional drainage (two transpapillary and two additional transmural). In the conversion rate, we found a statistical difference favoring transpapillary approach ($p = 0.047$), but we had no randomization and the numbers are far too small to give any solid data on this. Surgery was necessary on one for a bleeding complication after series of therapeutic interventions: PPC in the pancreatic tail following AP received a pancreatic stent. PPC infection ensued, and a pseudocystogastrostomy was placed. PPC hemorrhage followed resulting in coiling of the splenic artery. Eventually, the infected PPA ruptured and re-bled intraperitoneally. Pancreatic tail resection with splenectomy was necessary. After the resection, patient needed pancreatic duct stenting due to fistula.

Control imaging scheduled 10 (3–75) weeks after successful initial endoscopy showed complete resolution of a PPC in 30 of 32 (93.8 %). Treatment with pancreatic stents lasted 15 (4–41) months. Spontaneous dislocation of pancreatic stents occurred with two patients. Post-endoscopy follow-up was discontinued at 15 (1–75) months. One of the patients whose PPC did not resolve after endoscopy had uneventful pancreatic duct stenting 16 weeks after successful coiling of a bleeding 3.4-cm splenic PPA, but died 29 days after ERCP for an unknown cause. The other had a bleeding complication necessitating surgery (patient described earlier).

Complication rate after endoscopic procedures was 20.6 % (Table 5). PPC infection was the most common complication seen in 4 (11.8 %) patients. All of these had

Table 5 Results: management of pseudocysts

Endoscopic treatment method used ($n = 32$) [n (%)]	
Pancreatic stent	24 (75.0)
Pseudocystogastrostomy	7 (21.9)
Pseudocystoduodenostomy	1 (3.1)
Need for re-intervention ($n = 32$) [n (%)]	7 (21.9)
Endoscopy	5
Surgery	1
Percutaneous drainage	1
Overall PC non-surgical management success rate ($n = 47$) [n (%)]	43 (91.5)
Resolution after endoscopy	30 (73.2)
Spontaneous resolution	13 (27.7)
Thirty-day morbidity, $n = 34$ [n (%)]	7 (20.6)
PC infection	4
PC hemorrhage during endoscopy	2
Pancreatitis	1
Thirty-day mortality, $n = 34$ [n (%)]	1 (2.9)
Patient dies <30 days post-ERCP, cause unknown	1
Timing of endoscopic therapy ($n = 34$) [n (%)]	
Before embolization	5 (14.7)
After embolization	29 (85.3)
Time from embolization to endoscopy (week)	4 (2–45)[a]
Time from embolization to spontaneous resolution of PC (week)	8 (5–44)[a]
Time from endoscopy to resolution of PC (week)	10 (3–75)[a]
Overall duration of treatment with pancreatic stents (months)	15 (4–41)[a]
Follow-up time (months)	15 (1–75)[a]

Five patients followed up in another hospital excluded from the analysis

PC pseudocyst, *ERCP* endoscopic retrograde cholangiopancreatography

[a] Median (range)

received an antibiotic prophylaxis prior to the endoscopic procedure. Two patients recovered with intravenous antibiotics. Two needed additional draining procedures: The first received an additional pseudocystogastrostomy, because the pancreatic duct stent was too short and not draining the PPC efficiently. The other received additional percutaneous draining. Hemorrhage during endoscopy occurred in two patients (5.9 %). The first had a bleeding during the insertion of pseudocystoduodenostomy necessitating embolization. This complication was potentially preventable had EUS been used. Following a series of treatment procedures, the other had an infected PPA rupturing into abdominal cavity and necessitating laparotomy (patient described earlier). Post-ERCP pancreatitis with a mild course occurred in one (2.9 %) and resolved with conservative measures.

Survival

Thirty-day mortality rate after embolization was 3.4 % ($n = 2$). One patient developed disseminated intravascular coagulopathy due to profuse bleeding and died after embolization on the operating table. One patient with chronic obstructive pulmonary disease died 8 days after embolization for pneumonia and acute respiratory distress syndrome. Thirty-day mortality after ERCP was 2.9 % ($n = 1$) the patient dying 29 days after ERCP for an unknown cause.

Our follow-up after the treatment procedures discontinued at 15 (1–75) months. By the end of the follow-up, 8 of the 58 patients died giving an overall mortality rate of 13.8 %. By the time of data retrieval, 35 of 58 patients had died. Kaplan–Meier analysis shows a 5-year survival estimate of 63 % (Fig. 4). Alcohol liver disease was the most common cause of death (12.1 %) followed by cancer (5.2 %). Chronic pancreatitis was the cause of death of two patients (3.4 %).

Discussion

Our data show an angioembolization success rate of 96.6 %. Non-surgical management of a PPC after embolization was successful in 91.5 %, including the

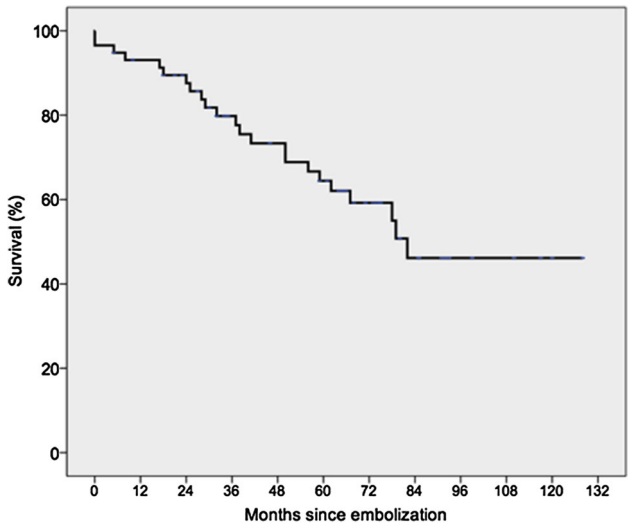

Fig. 4 Kaplan–Meier curve showing survival after embolization in patients with acute or chronic pancreatitis complicated by bleeding pseudoaneurysms or visceral artery aneurysms

endoscopically treated PPCs and the ones that resolved spontaneously. Severe complications were rare. Only 3 (5.2 %) patients required surgery: two for a re-bleeding episode and one for necrosis of cecum caused by post-embolization Ogilvie's syndrome. If left untreated, bleeding PPAs and VAAs have a mortality of up to 90 % [5]. No data on the long-term survival of these patients after the successful treatment of hemorrhage exist. To study this, we performed a Kaplan–Meier analysis that gave a 5-year survival estimate of 63 % (Fig. 4). This shows that a bleeding VAA or PPA with underlying pancreatitis is often a late manifestation of long-term alcohol abuse and degenerative way of life, and is, thus, associated with poor prognosis.

In recent studies with patients recruited after year 2000, TAE success rates reach 95–97 % [4, 6]. Our results are consistent with these findings, supporting the current recommendations to use TAE as the first-line treatment for bleeding PPAs and VAAs. Many earlier reports evaluating the safety and efficacy of TAE have included a mixed group of patients with various pancreatitis-associated bleeding complications, showing mortality rates up to 19–21 % after TAE [3, 8]. We included patients who had developed PPCs as a complication of AP and CP. None of our patients had acute necrotizing pancreatitis, which most likely explains our low 30-day mortality of 3.4 % after TAE.

We had 52 coiling, three stenting, two particle injection and only one plug placement procedures. Coils are safe and easy to use, and coiling is our standard method in TAE. Particle injections in the mesenteric arteries and celiac axis may be risky due to ischemic complications caused by particle spread, and in these arteries, particle injections should be used with caution. Stents and plugs are safe to use but stiff and inflexible and, thus, technically more challenging to position. Stenting also allows a transarterial approach when the visceral artery aneurysm is, e.g., in the superior mesenteric artery that cannot be coiled. We cannot draw any reliable conclusions on the post-embolization complication profile of different embolization methods due to the low numbers of stents, plugs and particle injections used.

Current study is the largest so far reporting the outcomes of non-surgical management of PPAs. Bhasin et al. [15] published their results with eight patients in 2013. Case reports from Elton et al. (1997) included three patients and from Sayilir et al. (2011) only one patient [16, 17]. Earlier reports by Bhasin et al., Elton et al. and Sayilir et al. have shown promising results concerning the conservative treatment of bleeding PPCs with combining endoscopy and TAE [15–17]. In their study on the efficacy of TAE in the treatment of PPAs in CP, Udd et al. [4] performed therapeutic endoscopy following TAE on 13 patients. None of these needed surgery for their PPCs within a 14-month follow-up. With larger study population and more extensive follow-up, our findings strengthen the existing evidence.

Our study bears all the known weaknesses of a retrospective study. In the modern era, cystoenterostomies are the standard of care with draining PPCs in many centers [24]. In our unit, however, we use pancreatic duct stenting in two out of three PPC drainage procedures, and the same trend can be seen with our study subjects with a history of bleeding PPAs (9 out of 32 received transmural drainage). This exception to the common practice should be kept in mind when reading our results. It is at least to some extent a result of the high prevalence of CP (79.3 %) in our material, transpapillary approach allowing simultaneous access to often-strictured pancreatic duct. When retrospectively analyzing the pre-ERCP CT scans, the transmural approach was an alternative for only four out of the 24 patients treated primarily with a pancreatic duct stent. With the remaining 20 patients, the PPCs lay far in the pancreatic tail (seven patients), had pancreatic tissue in between the gastrointestinal lumen and the PPC (five patients), were too far from the gastric or duodenal wall (four patients), or had vascular structures close to the PPC (two patients), precluding the transmural approach. Two patients had multiple PPCs that were all managed with transpapillary stenting. It is also worth pointing out that we excluded eight patients that received surgery as the first-line treatment, which could affect the generalizability of our results. A look into their patient files shows various reasons behind the decision to proceed directly to surgery: Angiography was negative with no bleeding site found on

four of the eight. Angiography showed anomalous arteries suspicious for malignancy with one, necessitating Whipple procedure. Interventional radiologist was not available in the hospital on one occasion. With two remaining cases, no rationale for direct surgical intervention without angiography was evident when reading the patient files.

Traditionally, negative angiography with no detectable bleeding site has indicated surgery. No published data solely on empirical embolizations of pancreatitis-associated bleeding complications exist. We performed empirical embolization on nine patients with no contrast extravasation or VAA detectable in angiography. Three of these patients re-bled, after which two underwent successful recoiling and one needed surgery. Incidence of re-bleeds was not higher in patients who received empirical TAE. Over the years, interventional radiologists have become more active in performing empirical embolizations that have become increasingly important in the treatment of PPAs on patients with negative angiographies. Major complications and organ ischemia (excluding splenic infarctions) are rare but still worth taking into consideration [25]. An alternative strategy for hemodynamically stable patients could be watchful waiting with careful monitoring and repeated angiography when re-bleeding occurs. Comparison and further studies on these approaches are necessary.

Optimal timing of therapeutic endoscopy after TAE remains unsolved. In the three reports already mentioned, patients received ERCP during the same hospital admission within a few days from the embolization [15–17]. We performed endoscopy on an outpatient visit 4 (2–47) weeks following TAE believing that this would reduce bleeding and infection complications. Depending on the underlying etiology, previous publications show a spontaneous regression of a PPC in 3–65 % of patients [26–29]. In our study, PPCs resolved spontaneously in 27.7 %, which also favors delayed endoscopic intervention.

Our findings show that combining TAE with therapeutic endoscopy is a safe and efficient approach for the definitive treatment of PPCs complicated by bleeding VAAs in AP or CP. TAE is associated with shorter hospital stays than surgery in the treatment of bleeding PPAs [4]. It is likely to be more cost-effective also when combined with therapeutic endoscopy for definitive treatment of PPAs. PPAs in AP and CP often appear in the context of alcoholism and other severe comorbidities increasing the risks for surgery. Non-surgical approach provides a less-invasive treatment method for this moribund group of patients. Last, proceeding to surgery is still an option, if non-surgical treatment fails. Prophylactic embolization is necessary for incidental VAAs and should precede therapeutic endoscopy when CT detects an incidental PPC with a VAA. We performed therapeutic endoscopy before TAE on five patients with a history of bleeding episode. Pre-endoscopy CT scans did not detect their VAAs. Acute bleeding occurred during two of these endoscopies, necessitating instant embolization.

In conclusion, bleeding PPAs require non-surgical management. Patients with PPAs or bleeding VAAs should receive a prompt angiography and embolization. Surgery is necessary only if embolization is not feasible or fails. Follow-up imaging with CT allows for determination of any remaining PPCs after embolization. Utilizing therapeutic endoscopy in managing such PPCs is safe and efficient and has a potential to save patients from the risks of pancreatic surgery. We need more data to give a solid recommendation on the optimal timing of the endoscopic procedures. Further research is also necessary to clarify the roles of empirical embolizations and watchful waiting after negative angiography.

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Compliance with ethical standards

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