

The challenge of pancreatic anastomosis

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Abstract

Background and aims Significant progress in surgical technique and perioperative management has substantially reduced the mortality rate of pancreatic surgery. However, morbidity remains considerably high, even in expert hands and leakage from the pancreatic stump still accounts for the majority of surgical complications after pancreatic head resection. For that reason, management of the pancreatic remnant after partial pancreatoduodenectomy remains a challenge. This review will focus on technique, pitfalls, and complication management of pancreaticoenteric anastomoses.

Materials and methods A medline search for surgical guidelines, prospective randomized controlled trials, systematic metaanalysis, and clinical reports was performed with regard to surgical technique and complication management of pancreatic anastomoses.

Results Pancreaticojejunostomy appears to be most widely performed, but pancreaticogastrostomy is a reasonable alternative. Postoperative treatment with octreotide can be recommended only for patients with soft pancreatic tissue, and neither stents of the pancreatic duct nor drainages have proven to effectively reduce anastomotic complications. Gastroparesis remains the most common complication after pancreatic surgery and should be treated conservatively. However, it may be a symptom of other local complications, such as anastomotic leakage, pancreatic fistula or abscess. All septic complications may finally result in late

postoperative hemorrhage, which requires immediate diagnostic workup and therapy. Today, interventional radiology has emerged as a standard tool in the management of local septic complications and bleeding. Therefore, relaparotomy has become less frequent and salvage pancreatotomy is now a rare procedure in case of local complications.

Conclusion The surgeon's experience with one or the other technique of pancreatic anastomosis appears to be more important than the technique itself.

Keywords Pancreaticojejunostomy · Pancreaticogastrostomy · Leakage · Pancreatic fistula · Septic hemorrhage

Introduction

Pancreatic surgery has improved dramatically within the past 15 years. While in the 1980s mortality rates after Whipple's procedure still exceeded 20%, today, mortality has been reduced to less than 5% in high volume centers. Some authors even report mortality rates as low as 0 to 3% (own experience 2001–2006: 2.3%) [1–12]. Due to improved security of the procedure, pancreatic head resection is also applied for the treatment of benign conditions like chronic pancreatitis, large adenomas, diverticula and benign periampullary tumors. Partial pancreatoduodenectomy has become a standard procedure, and the critical step in pancreatic surgery is no longer the resection itself but the reconstruction of the pancreaticoenteric anastomosis. This is highlighted by the fact that in spite of significantly reduced mortality, morbidity remains as high as 30 to 50%, even in large series (own experience: 30.4%) [1, 3, 4, 6, 8–10, 12–18]. Complications related to the pancreatic remnant, such as pancreatic fistula, anastomotic dehiscence,

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abscess formation, and septic hemorrhage are the main causes of morbidity and mortality following pancreatic head resection [1–4, 12, 15, 17, 19, 20]. Some authors have named the pancreatic anastomosis the “Achilles heel” of pancreatic surgery because it has the highest rate of surgical complications among all abdominal anastomoses [21]. The following article will focus on different reconstructive techniques after pancreatic resection as well as on management approaches for anastomotic complications.

The pancreatic remnant

Resection of the pancreatic head using the scalpel might be superior to diathermia, ultrasound dissection or stapler pancreatectomy [22]. However, management of the pancreatic remnant after partial pancreaticoduodenectomy is still controversially discussed. More than 80 different methods of pancreatocenteric reconstruction have been proposed, illustrating the complexity of surgical technique as well as the absence of a gold standard for all patients [20]. Simple closure of the pancreatic duct by ligation, fibrin, or tissue glue without performing a pancreatic anastomosis resulted in high rates of fistulas, pancreatitis, and postoperative insulin-dependent diabetes, and therefore has been widely abandoned [23, 24]. Anastomoses of the pancreatic remnant with the jejunum or the stomach are common practice [11, 20, 22, 25]. Numerous methods for pancreatojejunostomy and—to a lesser extent—for pancreatogastrostomy have been described, and the most important principles will be discussed here.

Pancreatojejunostomy vs. pancreatocoejunostomy

Pancreatic anastomosis using a jejunal loop is probably the most commonly used method of surgical reconstruction after pancreatic head resection [20, 22]. Apart from different positions of the jejunal loop (antecolic, retrocolic, retromesenteric) and other variants like the isolated loop technique (separate Roux-Y loops for biliary and pancreatic anastomosis) [26, 27], mainly two types of anastomosis can be performed. First, in so-called invagination anastomoses, the cross section of the pancreatic remnant is completely immersed into the jejunal loop. Second, in “duct-to-mucosa” anastomoses, the pancreatic duct is primarily sutured to the mucosa of the jejunal loop [21, 28–30]. Here, pancreatic secretion is drained only via the pancreatic duct [31–35] and the parenchymatous cross-section of the pancreatic stump is covered by the jejunal wall, which has to be fixed with a second suture line to the pancreatic capsula [36]. The invagination technique is also called pancreatojejunostomy, whereas pancreatocoejunostomy is

an alternative name for “duct-to-mucosa” techniques. However, prospective randomized trials have found no differences between both methods regarding fistula rates, morbidity, or mortality [28, 33].

Dunking vs. telescopic anastomosis

Since most complications after pancreatic head resection originate from the pancreatic cross-section (e.g., pancreatic fistula), several variants of invagination or “dunking” techniques have been developed. The advantage of covering all possible leaks and injuries of the pancreatic capsula by deep insertion of the stump into the loop is limited by the risk of ischemic pancreatitis and necrosis following extensive devascularization of the stump. Most authors deem mobilization by 1.5–2 cm to be sufficient [20, 35]. Out of concerns that overlapping mucosa might lead to fistula formation and that wound healing between the jejunal mucosa and the pancreatic capsule is impaired, various methods such as mucosectomy, cauterization of the mucosa [37], and so called “telescopic” anastomoses have been developed. In “telescopic” anastomoses, the jejunal loop is inverted so that the surface of the pancreatic remnant is now covered by serosa instead of mucosa. Jejunal inversion can be prepared in advance or it can be achieved simultaneously with suturing the anastomosis using multilayer stitches [38]. The first method bears the advantage that traction and shear forces at the pancreatic remnant can be avoided during invagination. The methods of “dunking” and “telescopic” anastomosis vary from simple “parachute” techniques to sophisticated three- and four-layer techniques [20, 29, 39]. The so called “binding anastomosis” in which a circular ligature is looped around the entire circumference of the anastomosis in order to balance differences in diameter between jejunal loop and pancreatic remnant is another option [37].

End-to-end versus end-to-side anastomosis

The problem of differing diameters between the jejunal loop and the pancreatic remnant in end-to-end anastomosis can only partially be resolved by mechanical distension or inversion of the loop and different suture or binding techniques. Therefore, end-to-side anastomoses are more and more favored over end-to-end anastomoses [20, 21]. Size and shape of the antimesenteric opening of the jejunal wall can be adjusted to the cross-section of the pancreatic remnant. Although numerous technical variants have been published, prospective randomized studies are rare [28, 33].

Pancreaticogastrostomy

Some authors have proposed pancreaticogastrostomy as an alternative to pancreaticojejunostomy, assuming that postoperative complications are less frequent [40–42]. Excellent blood supply to the stomach, easy surgical technique, accessibility for postoperative endoscopy, and separate drainage of biliary and pancreatic juice were considered advantageous. It appears, however, that bleeding from the anastomosis is a typical complication of this technique. Most comparative studies are retrospective analyses of different cohorts and therefore of limited value (Table 1) [11, 25, 42–52]. Furthermore, excellent results of pancreaticogastrostomy were often compared to unsatisfactory results after pancreaticojejunostomy with uncommonly high rates of fistula and mortality. These authors probably had more experience with gastric anastomoses. A recently published survey in Japanese hospitals found no difference between pancreaticojejunostomy and pancreaticogastrostomy for the rates of fistula, bleeding, abscess, and mortality in 3,109 patients after pancreatic head resection [22]. Three prospective randomized trials comparing the two methods have been published (Table 1) [11, 53, 54], and none of them found significant differences. Consequently, the surgeon's experience with one or the other technique appears to be more important than the technique itself.

Own technique

In our department, we use a modified end-to-side duct-to-mucosa technique, which was originally devised by Leslie H.

Blumgart, New York (Fig. 1). Three to four transpancreatic U-sutures are placed in addition to the “duct-to-mucosa” sutures to fix the jejunal wall on the pancreatic remnant. Herewith, the pancreatic cross-section is completely covered by jejunal serosa, and tangential shear forces at the pancreatic stump seem to be widely eliminated. Since the introduction of this technique in our department, postoperative rates of pancreatic fistulas and overall morbidity have been reduced significantly (unpublished data).

Drainage and stenting

All of the aforementioned anastomotic techniques can be combined with stenting or drainage of the pancreatic duct [31, 32, 34, 35]. Three different types of drainages need to be discriminated. The external jejunal loop drainage is an endoluminal transcuteaneous drainage that derives biliary and pancreatic juice from the anastomosis in order to prevent postoperative accumulation of aggressive fluids in the afferent loop. “Lost drainages” or pancreatic stents are short tubes which are inserted or sutured into the pancreatic duct and typically surpass the anastomosis by a few centimeters [33]. They are intended to splint the duct-to-mucosa anastomosis, to prevent accumulation of pancreatic juice in the pancreatic stump and to avoid direct contact of the juice with the anastomosis. The third option is an external drainage of the pancreatic duct, using a long but thin silicon tube, which directly inserts the pancreatic duct via the jejunal loop [32, 34]. In contrast to the “lost drainage,” this tube has to be removed after a while. Since none of the drainages and stents has proven to be of

Table 1 Clinical trials comparing pancreaticogastrostomy and pancreaticojejunostomy following partial duodenopancreatectomy

Author	Ref.	Year	Study design	Patients (n)	Pancreaticogastrostomy		Pancreatic fistula (%)	Morbidity (%)	Mortality (%)
					(n)	(%)	PJ/PG	PJ/PG	PJ/PG
Adloff et al.	[43]	1992	retro.	72	15	21	2/13	18/47	4/13
Miyagawa et al.	[48]	1992	retro.	52	21	40	19/5	45/57	6/0
Mason et al.	[42]	1995	retro.	58	34	59	17/0		13/6
Yeo et al.	[11]	1995	pro. rand.	145	73	50	11/12	45/49	0/0
Andivot et al.	[44]	1996	retro.	59	43	73	13/14	25/44	6/5
Kim et al.	[47]	1997	retro.	86	48	56	16/2	34/19	8/4
Arnaud et al.	[46]	1999	retro.	171	80	47	13/4	23/13	12/4
Takano et al.	[51]	2000	retro.	142	73	51	13/0	30/6	3/0
Schlitt et al.	[50]	2002	retro.	441	260	59	13/3	22/12	13/4
Aranha et al.	[45]	2003	retro.	214	177	83	14/12	81/55	4/0
Oussoultzoglou et al.	[49]	2004	retro.	250	167	67	20/2	63/38	2/3
Bassi et al.	[53]	2005	pro. rand.	151	69	46	16/13	39/29	1/0
Duffas et al.	[54]	2005	pro. rand. mult.	149	81	54	20/16	47/46	10/12

Ref. Reference; PJ pancreaticojejunostomy; PG pancreaticogastrostomy; retro. retrospective; pro. prospective; rand. randomized; mult. multicentric.

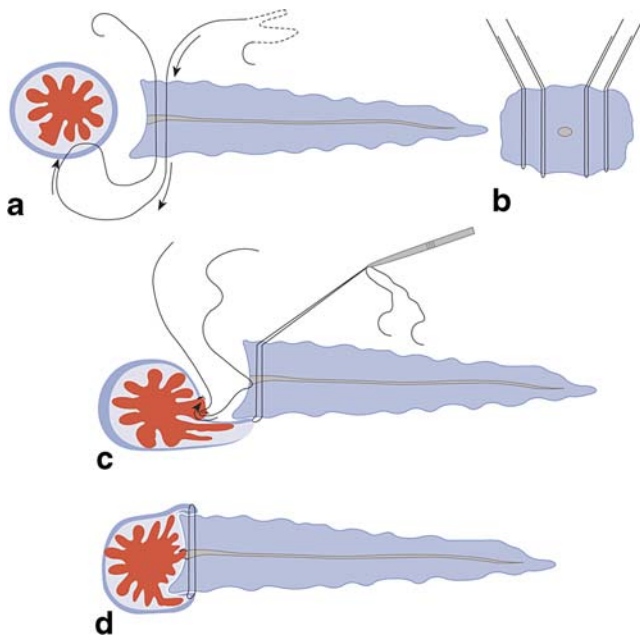


Fig. 1 Pancreaticojejunostomy as performed at the Surgical Department of Munich University, Klinikum-Grosshadern: an end-to-side “duct to mucosa” technique according to L.H. Blumgart, New York. Following 3–4 transpancreatic U-sutures, which approximate the posterior jejunal wall to the pancreatic remnant (**a**, **b**), the “duct-to-mucosa” anastomosis is performed by 4–8 single stitches (**c**). Finally, U-sutures are completed on the anterior wall of the loop (**d**). This technique avoids tangential shear forces on the pancreatic capsule and may reduce the occurrence of fistulas

significant benefit, but pancreatic duct drainages may cause acute postoperative pancreatitis of the remnant, their use has been concluded in our department.

Octreotide

Prophylactic use of somatostatin and synthetic somatostatin analogues (octreotide, vapreotide) during and after pancreatic surgery remains controversial [55]. The matter of interest is a suppression of exocrine pancreatic secretion to prevent postoperative complications [56, 57]. Until recently, however, it was not clear whether the suppression of exocrine pancreatic secretion significantly reduces the rate of pancreatic fistula. Several randomized, placebo-controlled multicentre trials came to contradictory results (Table 2) [58–62]. Only recently, Connor et al. published a meta-analysis of prospective randomized controlled trials with at least 50 included patients per trial (1,918 patients, 10 studies). The authors report that somatostatin analogues were able to reduce the rates of biochemical fistula, pancreas-specific complications, and overall morbidity but not the incidence of clinically relevant anastomotic disrup-

tion or mortality after pancreatic surgery [55]. Regarding pancreas-specific complications, one in nine patients (11%) did profit from the treatment with octreotide. Today, prophylactic treatment with octreotide is common practice in patients with soft pancreatic tissue, with a filiform pancreatic duct and without fibrosis, particularly in oncological surgery [own prophylactic regimen: 100 µg subcutaneously every 8 h for 5 days]. However, there are no clear data for this subgroup, and the decision should be left to the individual surgeon.

Delayed gastric emptying

Delayed gastric emptying (DGE) occurs in approximately 30% (10–70%) of patients after partial pancreaticoduodenectomy, and therefore is the most common complication after pancreatic head resection [1, 4, 5, 11, 12, 16, 63–67]. Defining DGE by the need of a nasogastric tube for more than 3 days following surgery or reinsertion of the nasogastric tube after day 3 appears reasonable because this significantly impairs postoperative oral intake [67]. A relationship to the preservation of the pylorus has not been established [63–67]. Likewise, problems with the gastrojejunostomy or pylorojejunostomy appear to be only rarely the cause of DGE. However, two recently published trials could demonstrate an association of DGE and retrocolic reconstruction of the pylorojejunostomy in patients undergoing pylorus preserving pancreatoduodenectomy [68, 69]. Therefore, the antecolic route for reconstruction should be recommended. If DGE occurs, the patency of the gastrojejunostomy or pylorojejunostomy should be confirmed and small bowel obstruction excluded, as mechanical complications need to be distinguished from gastroparesis [67]. The main causes of postoperative gastroparesis are extended retroperitoneal lymphadenectomy and abdominal septic complications, which need to be treated first [6, 65, 70, 71]. Gastro-duodenal denervation and decreased serum levels of motilin after duodenopancreatectomy may also play a role in postoperative gastroparesis, since motilin secretion is primarily located in the duodenum. DGE significantly prolongs hospitalization [11, 63, 67] but is not life-threatening and can most often be managed conservatively using erythromycin (an agonist on the motilin receptor), prokinetic drugs (e.g., metoclopramide, neostigmine), a nasogastric tube, and total parenteral nutrition [72].

Clinical management of anastomotic complications

Although gastroparesis is the most common complication after duodenopancreatectomy, leakage from the pancreatic

Table 2 Prospective randomized placebo-controlled trials for the value of somatostatin analogues after pancreatic surgery

Author	Ref.	Year	Study design	Patients (n)	Drug	Dose	Complications (%) T/P	Mortality (%) T/P	Significant
Pederzoli et al.	[60]	1994	Multicentric	252	Octreotide	100 µg, 3×/day, s.c.	16/29	2/4	Yes
Büchler et al.	[58]	1994	Multicentric	246	Octreotide	100 µg, 3×/day, s.c.	32/55	3/6	Yes
Montorsi et al.	[59]	1995	Multicentric	218	Octreotide	100 µg, 3×/day, s.c.	22/36	8/6	Yes
Yeo et al.	[62]	2000	single centre	211	Octreotide	250 µg, 3×/day, s.c.	40/34	1/0	No
Sarr et al.	[61]	2003	Multicentric	275	Vapreotide	600 µg, 2×/day, s.c.	40/42	0/1	No

T Treatment group; P placebo group

anastomosis with subsequent local sepsis is the major cause for postoperative morbidity and mortality [1, 3–5, 8, 12, 14, 19, 45]. In the following, the diagnostic and therapeutic approach to pancreatic fistula, anastomotic breakdown, abscess formation, and septic hemorrhage will be discussed. During the last decade, further development of interventional radiology has led to a more conservative management of septic complications. Most high volume centers report only slightly decreasing rates of postoperative complications, but a significant reduction in relaparotomies [7, 10, 12, 14, 16].

Pancreatic fistula and anastomotic dehiscence

Definition

The terms pancreatic fistula, pancreatic leakage, and anastomotic dehiscence are not unequivocally defined in the literature. All terms signify a leakage in the area of the pancreatic anastomosis and could, therefore, be used synonymously. Contrary definitions and usage of these terms, however, have led to confusion. Hence, diverging rates of postoperative fistula (1–24%) were reported by different teams that use the same surgical technique [1, 4, 10, 12, 15, 19, 29, 73]. A uniform definition is therefore urgently needed to make results comparable. It appears reasonable to discriminate a biochemical fistula from anastomotic breakdown. We define pancreatic fistula as a persisting amylase-rich effluent via upper abdominal drainages for more than 3 days after surgery (> 10 ml/day containing threefold levels of serum-amylase) [74]. Anastomotic breakdown, though, should only be diagnosed when clinical signs of abdominal sepsis are apparent (increasing pain, peritonism, fever >38.5°C, leukocytosis >15×10⁹/l and evacuation of infected fluid or intestinal content via local drains) or leakage is radiologically or operatively verified. In general, pancreatic fistula is not

dangerous and occurs in up to 20% after pancreaticojejunostomy [45, 48, 49, 75]. Clinical relevant anastomotic disruption is less common but critical since it constitutes the primary cause of postoperative mortality [2, 7]. Large trials have shown mortality to be as high as 40% when anastomotic dehiscence is present [1, 3, 9, 12]. In case of survival, therapy is complicated, and hospital stay is prolonged.

Etiology

Various risk factors for anastomotic dehiscence and pancreatic fistula have been described. It is generally accepted that tissue consistency, exocrine function of the pancreatic remnant, and the diameter of the pancreatic duct are important determinants of pancreatic fistula [76–78]. Bartoli et al. reviewed 2,664 patients with postoperative pancreatic fistula with respect to the primary diagnosis [76]. Only 5% of patients with chronic pancreatitis, concomitant pancreatic fibrosis and exocrine insufficiency developed postoperative pancreatic fistula, while this rate was 12% for patients with pancreatic carcinoma, 15% for ampullary carcinoma and 33% for distal bile duct cancer. In the latter group, the pancreatic duct should not be distended at all. Therefore, the rate of pancreatic fistula was higher in patients with small duct and minimal fibrosis. Technical differences in anastomosis and drainage are thought to influence the rate of pancreatic fistula and have been discussed above. Results in the literature, however, are not consistent, and the choice of surgical method should be based on individual experience. Nonetheless, general surgical skill does matter in the prevention of pancreas-specific complications. Preparation and resection of the pancreas should be done with extreme care and any unnecessary manipulation and mobilization should be avoided. Furthermore, we believe that shear forces on the anastomosis through tangentially placed sutures may promote pancreatic leakage, and that transpancreatic U-

sutures as applied for the Blumgart anastomosis (Fig. 1) and other mattress techniques [33] might be a reasonable strategy to prevent pancreatic fistula.

Diagnosis

Most pancreatic fistula and anastomotic disruptions occur 3 to 7 days postoperatively, and early diagnosis is crucial. Patients sometimes complain about dyspnea, tachycardia, and progressive abdominal pain (in case of anastomotic dehiscence) but may show just as well only weak symptoms like gastroparesis, bowel atony, or be completely asymptomatic (in case of pancreatic fistula). Proper physical examination is fundamental to the detection of anastomotic dehiscence. An increase in pancreatic secretion that becomes milky before turning turbid brownish is a characteristic finding. Plain abdomen and chest radiographs may hint at abdominal sepsis by showing ileus or pleural effusion. The latter occurs in 75% of patients with anastomotic dehiscence following pancreatic surgery [79, 80]. Free abdominal air, however, is a rare finding and indicates a serious anastomotic breakdown. In the early phase of anastomotic failure, CT scan often shows unspecific changes like pancreatic edema and peripancreatic fluid collections. However, late complications such as abscess formation or septic pseudoaneurysm of visceral arteries can easily be diagnosed with CT scan. In some cases, even the application of a contrast agent via the peritoneal drain may reveal a necrotic cavity or even the anastomotic dehiscence itself (Fig. 2).

Therapy

Therapeutic strategies for pancreatic fistula and anastomotic dehiscence have changed in recent years. Today, treatment

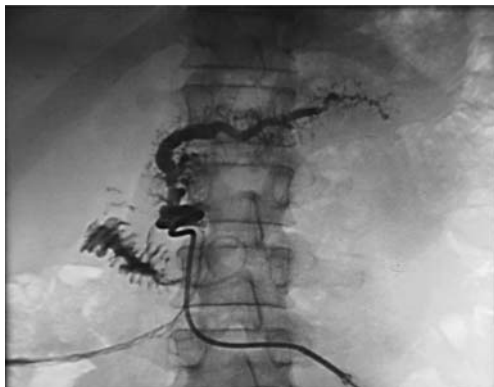


Fig. 2 Contrast medium given through a peritoneal drainage displays the anastomotic dehiscence after limited pancreatic head enucleation and longitudinal pancreaticojejunostomy according to Frey. The anastomotic leakage was well drained and could therefore be treated conservatively. Jejunal loop, drainage and distended pancreatic duct can be identified

is individualized, depending on the clinical state of the patient [7]. In 80% of cases so-called “low output” fistula are present, which are mostly asymptomatic and should be treated conservatively with drainage, irrigation, and temporary TPN or nutrition through a feeding jejunostomy for 2–3 weeks [81]. Proper fixation of peritoneal drainages is crucial to prevent their accidental loss. A follow-up CT scan might be useful to exclude late abscess formation. Experienced groups report fistula rates of 9–15%, but surgical intervention is required in only 4% of patients [1, 7]. Percutaneous CT-guided drainage has significantly reduced the rate of relaparotomies [82–84]. Only a small group of patients develops abdominal sepsis and needs another surgical procedure. Intraoperative management depends on the clinical state of the patient, the vitality of the pancreatic remnant and the degree of anastomotic dehiscence. Nowadays, completion pancreatectomy is only rarely performed [1]. In case of a sufficient anastomosis but a small fistula of the pancreatic tail or a small leakage of the anastomosis, irrigation and insertion of additional drains into the lesser sac is the proper clinical approach (similar to acute pancreatitis). In the case of anastomotic disruption or subtotal dehiscence, surgical repair of the anastomosis should usually not be attempted because blood supply is often not adequate and the inflammatory tissue cannot be securely sutured. In these cases, the anastomosis should be resolved and the jejunal loop shortened and closed [1]. In some cases, when extensive necrosis is present, salvage pancreatectomy including splenectomy is the only life-saving option, and it should be done before septic shock develops [71, 79, 85, 86]. However, the hospital mortality for those patients still remains high [1]. If the pancreatic tail shows no signs of major pancreatitis or necrosis, shortening and closure of the pancreatic stump and extensive surgical drainage can be performed [87]. This approach may lead not only to a reduction in postoperative diabetes but also to a higher incidence of pseudocysts. Only in selected cases of early technical failure, suturing a new anastomosis is feasible. For this procedure, the absence of local sepsis and a sufficient blood supply are obligatory [88].

Biliary fistula

Dehiscence of the bilioenteric anastomosis and consequent biliary fistula are rare (1–9%) and can usually be managed conservatively by adequate drainage. Only in some patients percutaneous transhepatic drainage of the biliary system is necessary in addition to maintenance and irrigation of intraoperatively placed peritoneal tubes. Using combined intra- and extraluminal biliary drainage, the fistula generally closes spontaneously. Surgical intervention is usually

not necessary and limited to major leakage during the first postoperative days caused by technical problems [6, 7, 14, 81, 85, 89]. Late onset of septic bilioma should be treated by CT-guided drainage and irrigation.

Abscess

Intra-abdominal abscess formation occurs in approximately 10% of patients following duodenopancreatectomy, mainly as a consequence of pancreatic fistula or dehiscence of the pancreatic anastomosis [6, 7, 14, 81, 85, 89]. A real abscess should not be confounded with early postoperative fluid collections diagnosed on CT scan. Fluid collections occur frequently and regress spontaneously after a few weeks without any specific therapy. Biliary fistula and dehiscence of the gastrointestinal or entero-enteric anastomosis are rarely the cause for postoperative abscesses. Principally, CT or ultrasound-guided drainage and i.v. antibiotics are the therapy of choice. With respect to potential secondary complications, any abscess diagnosed must be drained. Only if an abscess cannot be drained sufficiently by interventional radiology or if the patient does not improve in spite of sufficient drainage, surgical intervention may be necessary to prevent further complications.

Postoperative bleeding

Bleeding occurs in around 2–18% of patients after pancreatic surgery [1, 12, 14, 64, 66, 90–95] and is associated with a mortality rate of 15–60% [81, 85, 90, 92, 94–96]. Different causes may be responsible. We should discriminate early from late postoperative bleeding and abdominal from gastrointestinal (intraluminal) bleeding [95]. Based on the onset, localization and severity of bleeding the International Study Group of Pancreatic Surgery (ISGPS) has recently proposed a classification of postpancreatectomy hemorrhage (PPH) into three grades. PPH grade A is defined as a mild early postoperative bleeding without major clinical impact, PPH grade B as a severe early postoperative bleeding with a consecutive change in a given clinical pathway, and PPH grade C as a severe late postoperative hemorrhage with immediate diagnostic and therapeutic consequences [95].

Early abdominal bleeding

Early abdominal bleeding is the most frequent type of postoperative hemorrhage (PPH grade A/B). It occurs within 24–48 h after surgery and is usually caused by

either inadequate hemostasis or a slipped ligature. Technical causes are responsible for 30–60% of cases [90, 92]. Nonetheless, coagulopathies, e.g., due to major intraoperative blood loss or preoperative hyperbilirubinaemia, might also be responsible for diffuse postoperative hemorrhage. In large series, however, no significant difference in bleeding rates between patients with or without jaundice was found. For that reason, the advantage of preoperative biliary decompression is questionable [92]. Early abdominal bleeding can be easily detected through early blood loss via the peritoneal drainages, a drop in hemoglobin levels and alteration of vital signs. Depending on the intensity of bleeding and the patient's cardio-circulatory function (PPH grade A/B), blood transfusions and pro-coagulatory drugs are combined with timely surgery for hemostasis and removal of hematoma [7, 90, 92].

Early gastrointestinal bleeding

Early gastrointestinal bleeding may appear as coffee ground vomitus, change of color in the naso-gastric tube or melena. Depending on severity, the bleeding can be associated with a drop in hemoglobin levels or with hemorrhagic shock. Postoperative GI-bleeding is usually caused by mucosal bleeding or bleeding from the suture-line of the gastrointestinal or pylorointestinal anastomosis, and can be controlled endoscopically in most cases [90]. Early bleeding from the pancreaticojejunostomy or the bilioenteric anastomosis is rare [97], and postoperative stress ulcer bleeding is—contrary to the common belief—extremely rare after duodenopancreatectomy [92]. Immediate but cautious endoscopy is the diagnostic and therapeutic approach of choice (Fig. 4a). In most cases, anastomotic bleeding can be controlled endoscopically by injection of fibrin glue, sclerosants or application of clips [90]. Relaparotomy only has to be performed in cases of insufficient hemostasis despite endoscopic treatment, limited cardio-circulatory function, unknown origin of GI-bleeding due to large amounts of endoluminal blood or suggested bleeding from the afferent loop (Fig. 4a) [97]. Intraoperatively, most endoluminal bleedings can be controlled directly via gastrotomy proximal to the gastro-enterostomy. Some authors also report good results for enterotomy of the jejunal loop in case of bleeding from the pancreatic or biliary anastomosis [92, 97].

Late postoperative bleeding

Late postoperative bleeding is a rare (1.5–5%) but serious complication after pancreatic surgery (PPH grade C) [7,

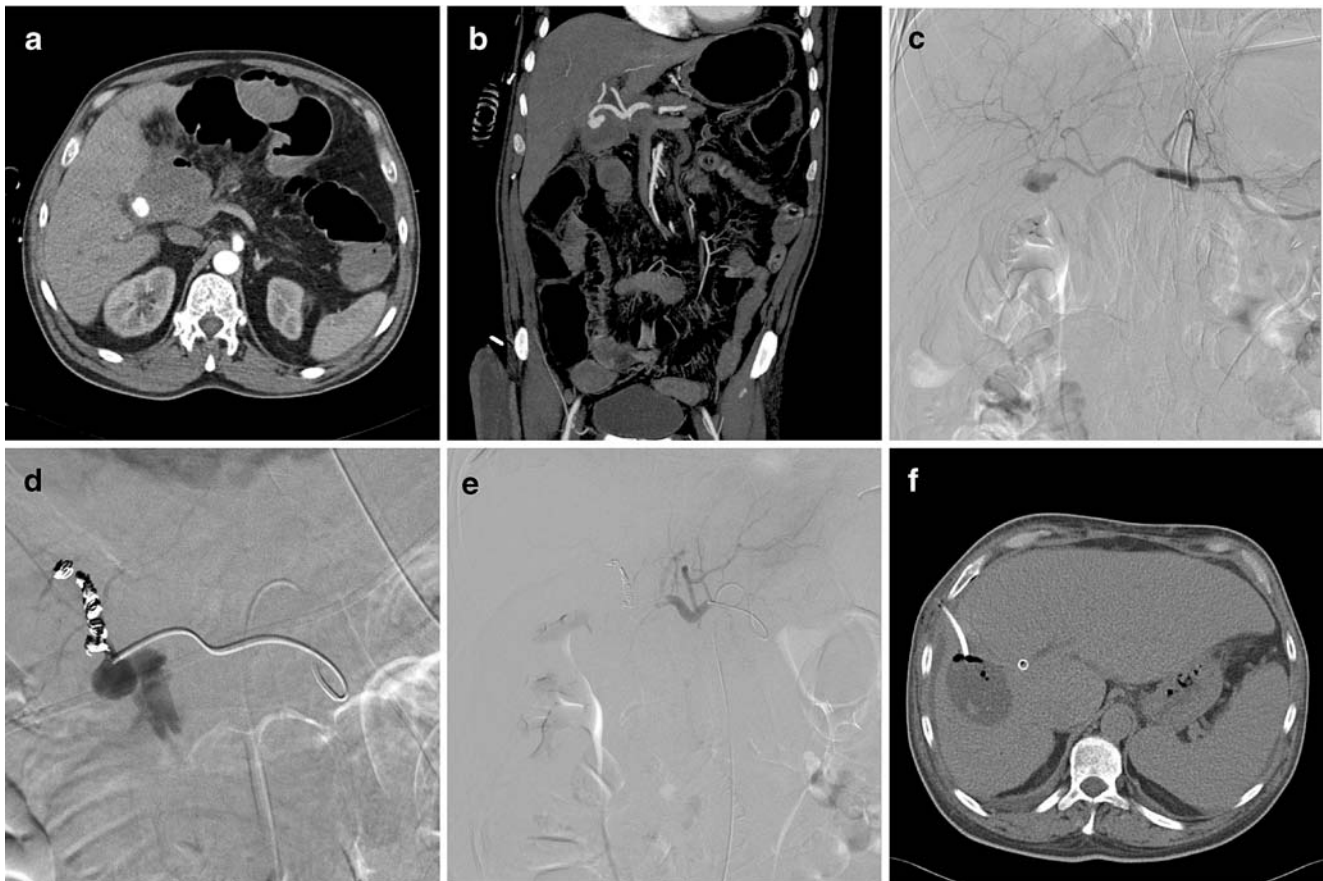


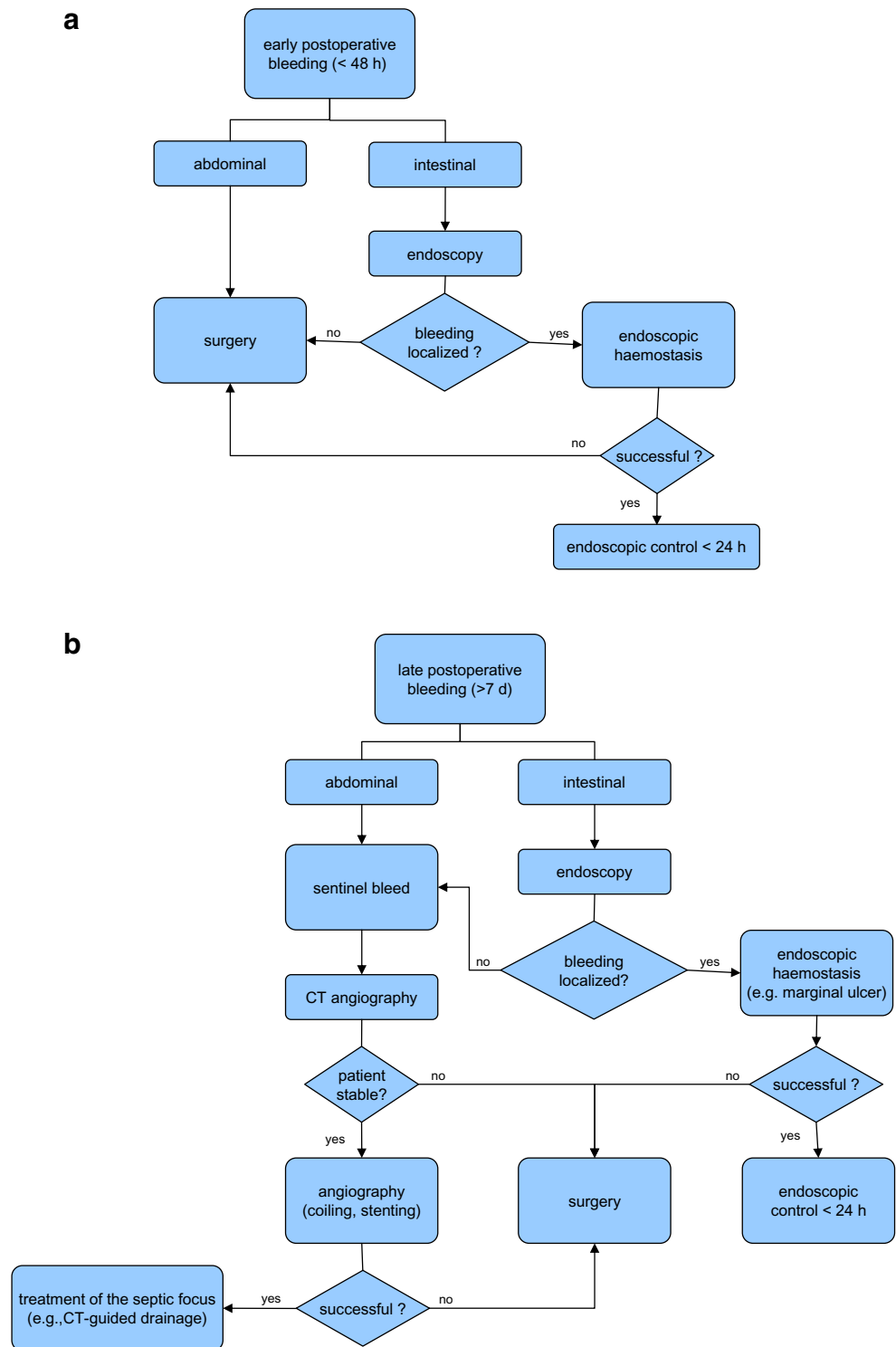
Fig. 3 Erosive bleeding from the right hepatic artery due to a sub-hepatic abscess 4 weeks after Whipple's procedure (PPH grade C) (a, b). Drop in hemoglobin levels and cardio-circulatory instability of the patient led to the diagnostic work-up with primary CT-scan (a, b) and immediate angiography of the celiac trunk for precise localization

of the bleeding (c). Selective catheter-embolization distal (d) and proximal to the site of erosion was achieved, with final occlusion of the right hepatic artery (e). CT-guided drainage of the sub-hepatic abscess could initially avoid surgery, but as a consequence of coiling a second intrahepatic abscess developed due to ischemia (f)

98–100]. It is defined as postoperative hemorrhage more than 48 h after surgery and is associated with a mortality rate higher than 60% [90, 92–94, 99–102]. If the bleeding occurs intraluminally, the pancreatic anastomosis or marginal ulcers should be considered as the source of bleeding [90, 93, 94, 97, 101]. Most often, however, late postoperative bleeding occurs as abdominal hemorrhage due to local septic complications with consecutive erosion of large retroperitoneal vessels [92, 98, 100–103]. The hepatic artery or the stump of the gastroduodenal artery are regularly involved [99, 100]. Dissection of major vessels during lymphadenectomy in tumor patients [90, 99, 100] as well as neoadjuvant radiochemotherapy [104] are suggested risk factors. The dissected vessels are prone to erosion in a septic environment, especially when pancreatic fistula or anastomotic leakage is present. Septic pseudoaneurysm (e.g., of the gastroduodenal artery) or rupture (e.g., of the hepatic artery) can be the consequence. Pancreatic fistulas are found in up to 90% of

patients with late postoperative hemorrhage [92, 99, 101, 103]. Biliary fistula or dehiscence of the bilioenteric anastomosis is a less common cause of septic hemorrhage. Pre-existing chronic inflammatory pseudoaneurysms might be involved in late postoperative bleeding after surgery for chronic pancreatitis, where no lymphadenectomy was performed. No association could be established between the occurrence of bleeding and the placement of drainages [105]. However, prophylaxis seems to be the best therapy. Anastomotic leakage needs to be diagnosed early and drained sufficiently, late abscesses have to be treated by CT-guided drainages and irrigation, and all patients with diffuse peritonitis need manual irrigation in the operating theatre. Some authors have suggested a subtotal pancreatic resection shifted to the left with removal of the head and corpus instead of classical Whipple's procedure in order to avoid contact between major blood vessels and the pancreatic anastomosis [104]. Others have proposed covering of the vessels with the

Fig. 4 Diagnostic and therapeutic algorithm for early (a) and late (b) postoperative bleeding after pancreatic surgery (University of Munich, Klinikum-Grosshadern)



falciform ligament [90] or omentum [101, 106]. Suturing of the gastroduodenal artery instead of ligation and preserving a vessel stump of no less than 1 cm are recommended to avoid slipping of the knot in the presence of local sepsis and to allow catheter-embolization of the gastroduodenal artery in case of bleeding later on [100, 104].

Diagnosis

Bloody secretion via maintained peritoneal drainages days to weeks after surgery, suddenly deteriorated vital signs of the patient, and spontaneous drop in hemoglobin levels are highly suspicious of a late septic hemorrhage. Early diagnosis of a so-called “sentinel bleed” is very important

[101] because in 30 to 80% of patients, this little bleeding episode will precede a massive erosive hemorrhage by several hours or days [90, 99, 101, 103–105]. Particularly due to undetected septic complications like silent anastomotic breakdown or an undiscovered abscess, late anastomotic bleeding or preliminary septic hemorrhage may occur as a “sentinel bleed” and find its way either via the maintained drainages or via the dehiscence anastomosis into the intestine. This way, it may mimic upper GI-bleeding. Consequently, late gastrointestinal bleeding is always suspect of an anastomotic failure and a local septic complication, which needs immediate diagnostic workup [92]. If the source of bleeding cannot be identified endoscopically, a “sentinel bleed” must be suspected and its origin needs to be urgently sought after by contrast-enhanced high-resolution CT scan (Fig. 4b) [99–101]. Interventional angiography may follow for precise localization of the bleeding and catheter-embolization (*coiling/stenting*; Fig. 3) [99, 100, 102, 105].

Therapy

Angiography and interventional hemostasis (*coiling, stenting*) are preferable to open surgery in patients with stable cardio-circulatory conditions (Fig. 4b) [99, 100]. Surgery, in the scenario of late septic hemorrhage, is associated with high mortality and should be limited to patients with hemorrhagic shock or patients where embolization was not sufficient [7, 90, 92, 98, 105]. Several studies have demonstrated good results for catheter-embolization of septic bleeding in acute pancreatitis as well as in patients after partial pancreatoduodenectomy [99, 100, 103, 107, 108]. Success of this method, however, largely depends on local availability and expertise. Often, complete coiling of the eroded vessel (e.g. the hepatic artery) is necessary. This in turn may lead to secondary complications such as liver necrosis, hepatic abscess and biliary complications [99], particularly when accessory vessels are absent (Fig. 3f). In near future, stenting of the celiac arteries may possibly prevent this [109]. However, interventional hemostasis has to be followed necessarily by causative treatment of the septic focus. For that reason, some authors still prefer open surgery as the first-line therapy to interventional “bridging” [92, 98]. On the other hand, mortality of surgical revision in case of late septic hemorrhage remains high and the intraoperative management is still a matter of debate [98]. In most patients, hemostasis may only be achieved through ligation of the whole blood vessel concerned, which may lead to severe ischemic consequences, as described above. Some authors perform salvage pancreatectomy in the same session, for definite control of the septic focus [2, 79, 90, 110]. This benefit might be counterbalanced by the disadvantage of a large surgical trauma and postoperative

insulin-dependent diabetes [92]. Figure 4 shows our department’s diagnostic and therapeutic algorithm for postoperative bleeding following pancreatic surgery.

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