# Commentary

# 3

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## 3.1 Relevant Basic Information, Indication and Contraindication

Diagnosis of pancreatic cancer is usually made by high-resolution, thin sliced, contrast-enhanced, multiphase Computed tomography (CT) as the standard tool. We use magnetic resonance imaging (MRI) only in situations when CT cannot be performed (e.g. due to contrast medium allergy/renal failure). Our initial approach is, thus, comparable to the standard procedure in Magdeburg. Evaluation of the pancreatic tumor by CT can be done with a high local resolution that allows very accurate imaging of soft tissue and vascular structures, as well as the presence/absence of liver metastases. To improve quality, the CT protocol includes the so-called "hydro-technique" (Grenacher and Klauss 2009) which involves oral water intake (one liter or more) and the intravenous administration of buscopan (10 mg) prior to the examination to achieve maximum distension of the stomach and duodenum, thereby achieving a negative contrast inside the lumen. In addition, the patient is placed in an oblique, 30°, right-sided down position (Fig. 3.1).

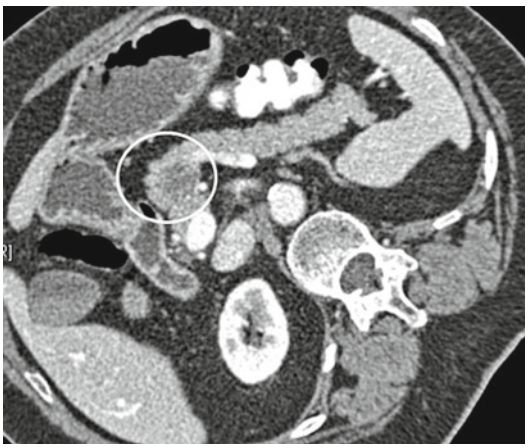

**Fig. 3.1** High-resolution CT scan, hydro technique with 30° right-sided position of the patient showing a hypodense tumor in the pancreatic head (*white circle*)

Criteria for resectability are the absence of metastases (liver/peritoneal) and no evident involvement of the central arterial vessels (celiac trunk, superior mesenteric artery). In the latter case, neoadjuvant treatment is initiated with the aim of downstaging the disease for a potential secondary resection. Portal and mesenteric vein involvement are not necessarily regarded as a contraindication, regardless of the extent of tumor infiltration.

Further diagnostic procedures, such as endoscopic ultrasonography and ERCP, are not mandatory. We do not favor stent placement in the bile duct unless the serum bilirubin levels exceed 300 µmol/l, which is usually associated with impairment of liver function and especially coagulation (van der Gaag et al. 2010). In contrast, when the operation has to be postponed because

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of cholangitis, neoadjuvant treatment, or need for more medical evaluation and treatment, cholestasis should be relieved before the operation. In these situations, a stent is inserted by endoscopic techniques or transhepatically, and the operation is delayed until the serum bilirubin decreases to <150 µmol/l. Most other patients are operated as soon as possible.

Preoperative tissue diagnosis by endoscopic or percutaneous five needle aspiration is only required in patients who are scheduled for neoadjuvant or palliative treatment, or if the nature of the tumor remains unclear (e.g. no increase in serum CA 19-9 level or unclear radiologic findings).

Concerning patient age, we have no routine cutoff, although 80 years represents a relative age after which a more critical reflection of the patient's condition, symptoms, and perioperative risk profile are considered (Makary et al. 2006). Biologic age and co-morbidities of the patient become the major factors that determine the decision for operative exploration or alternative palliative treatment in case of contraindications that are not directly tumor-related.

## 3.2 Operative Technique

Our standard approach to pancreatic head neoplasms is the pylorus-preserving partial pancreatoduodenectomy. We perform >90 % of all head resections with preservation of the pylorus; a classic pancreatoduodenectomy procedure with antrectomy is limited to patients with tumor spread toward the pylorus, suspicious lymph nodes in this area, or a history of peptic ulcers. The incision is not standardized. A midline laparotomy is preferred in non-obese patients, because this incision provides a more comfortable exposure during the phase of pancreaticojejunostomy; however, in obese patients, a transverse incision offers better exposure during the resection.

Regarding the resection itself, two approaches have been developed and are used increasingly in our clinical routine. The "standard" resection can be facilitated by the "uncinate-first approach" (Hackert et al. 2010), which involves the retrograde resection of the pancreatic head. The rationale for this approach is to begin the resection at the first jejunal loop with transposition of the specimen to the right aspect of the celiac axis. The resection is then carried out caudo-cranially under optimal vision of the superior mesenteric vein and artery to allow clear margins and excellent control of potential bleeding. From our experience, this is a very convenient and safe procedure.

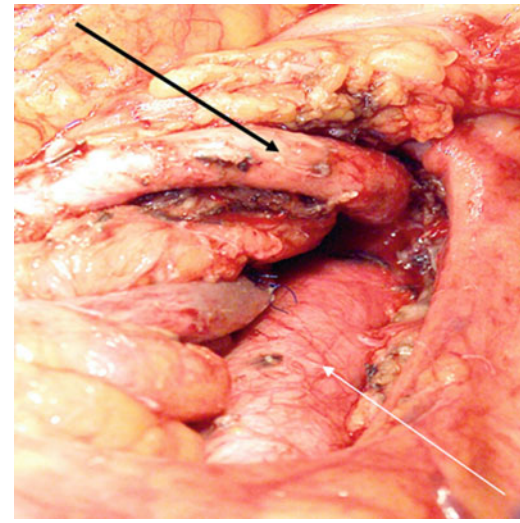

**Fig. 3.2** "Artery-first approach" with exposition of the superior mesenteric artery from the left side (*black arrow*: superior mesenteric artery; *white arrow*: aorta)

The second newer technique is the "artery-first approach" (Weitz et al. 2010). The essential step during this procedure is dissection of the superior mesenteric artery beginning from the left side of the mesenteric axis. The artery is exposed down to its origin so that tumor adherence can be excluded safely and before any other definitive steps of the resection have taken place (Fig. 3.2). This approach is especially appropriate in patients in whom arterial involvement remains unclear in the preoperative evaluation.

Transection of the neck of the pancreas anterior to the portal vein can be performed before completing the dissection along the portal vein or may be done as the last step of the procedure. We prefer to place sutures at the superior and inferior pancreatic margin on both sides of the transection line. This maneuver offers control of bleeding from the vessels in these regions and can be used to lift up the pancreatic remnant during the further mobilization of the body of the gland. We do not use electrocautery for control of bleeding on the

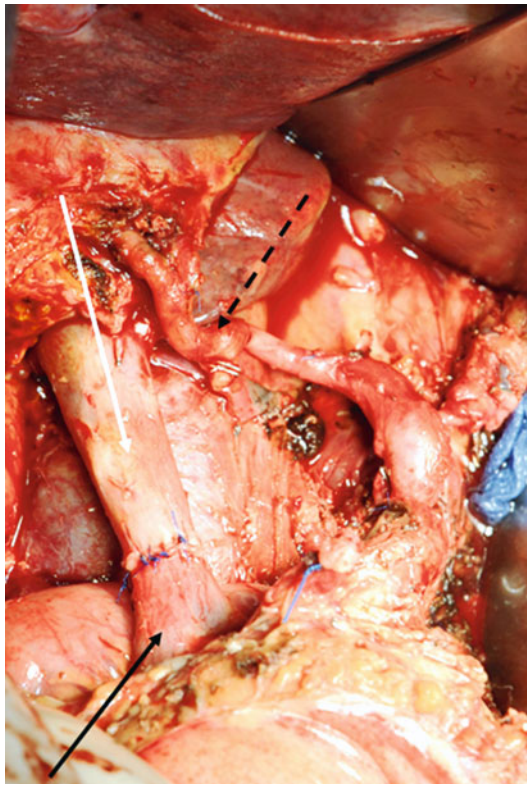

**Fig. 3.3** Portal vein reconstruction during total pancreatectomy. End-to-end anastomosis between superior mesenteric vein (*black arrow*) and portal vein (*white arrow*), *broken black arrow*: proper hepatic artery

cut surface of the remnant; instead, atraumatic, non-resorbable sutures are the standard for this step of the operation.

When there is involvement of the superior mesenteric or portal vein, we prefer a reconstruction by direct suture of the vein, either as mentioned in the Magdeburg approach by a lateral venorrhaphy, or when necessary, by an end-to-end anastomosis. For both techniques, non-resorbable suture material (e.g. 5-0 polypropylene) is used with intraoperative assessment of blood flow after the reconstruction (Fig. 3.3). From our experience, a venous or synthetic graft is rarely necessary. To gain enough mobility of the distal superior mesenteric vein for a tension-free anastomosis, it is essential to mobilize the root of the mesentery completely. This technique is accomplished by dividing the attachment of the mesentery of the ileum and right colon from the retroperitoneal plane up to the base of the small bowel mesentery with antero-rostral elevation of the small bowel. After complete mobilization, portal vein defects of 4–5 cm can usually be bridged without any tension.

Our standard lymphadenectomy during partial pancreatoduodenectomy includes the lymph nodes in the hepatoduodenal ligament (group 12), and those nodes along the common hepatic artery (group 8), portal vein (group 12), and the cranial portion of superior mesenteric vein (group 4–6), as well as right-sided lymph nodes of the celiac trunk (group 9) and the right side of the superior mesenteric artery (group 3) (Adler et al. 2007; Japan Pancreas Society 2003).

The impact of extended lymph node dissection (i.e. paraaortic nodes in the aortocaval groove, left-side of the celiac trunk, and the left side of the superior mesenteric artery) has been well investigated in four, randomized, controlled trials between 1998 and 2005 examining survival (Pedrazzoli et al. 1998; Yeo et al. 1999; Farnell et al. 2005; Nimura et al. 2004). Although there were differences in the studies with regard to the number of resected lymph nodes (20 vs. up to 40), three of the studies showed no survival advantage, either in N0 nor in N1 patients who underwent a standard or extended resections. Only Pedrazzoli et al. (1998) found a survival benefit of 7 months in the subgroup analysis for N1 patients who underwent extended resection. Moreover, all groups except for Pedrazzoli et al. observed a markedly increased morbidity and decreased quality of life in the postoperative follow-up related to diarrhea, nutritional difficulties, etc. A metaanalysis published in 2007 (Michalski et al. 2007) analyzed these studies – including an overall number of 297 vs. 311 patients – with regard to their scientific quality and results. No benefit for such an extended lymphadenectomy could be determined concerning either local tumor control or survival. Furthermore, an increased rate of perioperative complications and a decreased quality of life were demonstrated. Therefore, with regard to these studies and consequently based on a level 1 evidence, the concept of ultra-radical lymphadenectomy should be abandoned, and a defined standardized lymph node

dissection should be performed during partial pancreatoduodenectomy (Fig. 3.4).

We maintain that the most important operative step in preventing severe postoperative complications is the pancreaticojejunostomy. We prefer to perform the anastomosis end-to-side in a two-layer fashion suturing the pancreatic duct separately (Figs. 3.5, 3.6, and 3.7). Three atraumatic, resorbable sutures are placed at the anterior and posterior aspect of the pancreatic duct at the beginning. These sutures are later integrated in the inner suture row. The outer row is performed with interrupted, 5-0 PDS sutures between the pancreatic capsula and the seromuscular layer of the jejunum. After incision in the jejunal wall, the second back row is performed with interrupted sutures which incorporates the previously placed posterior ductal stitches. The anterior wall of the anastomosis is sutured in a similar fashion with two layers of interrupted stitches. We do not use intraductal stents in the pancreatic duct because of concerns that they tend to obstruct the outflow in small diameter ducts. Using our technique, rates of Grade Band C leaks occur in about 3 % (Büchler et al. 2003; Wente et al. 2006). Bile duct reconstruction is standardized by a one-layer, end-to-side technique using resorbable monofilament sutures approximately 10–15 cm distal to the pancreatic anastomosis to minimize the risk of bile reflux toward the pancreas. An end-to-side duodenojejunostomy completes the reconstruction. Recent studies have shown that an antecolic reconstruction is more favorable in terms of preventing delayed gastric emptying (Hartel et al. 2005). Two closed suction drains (12 mm, EasyFlow®) are used routinely and positioned near the pancreatic anastomosis and in the subhepatic space from the right side of the abdomen. Drain removal, which can usually be done

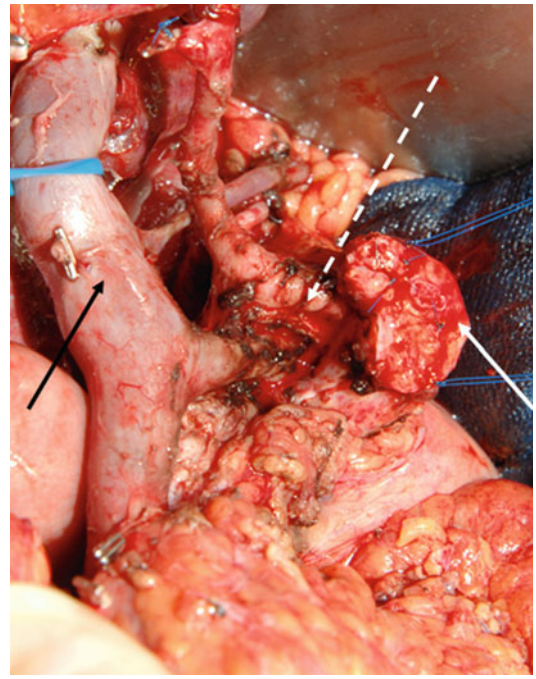

**Fig. 3.4** Situs after partial duodeno-pancreatectomy with standardized lymphadenectomy. Dissection has been performed along the portal vein (*black arrow*) and right side of the celiac axis (*broken white arrow*), *white arrow*: pancreatic remnant

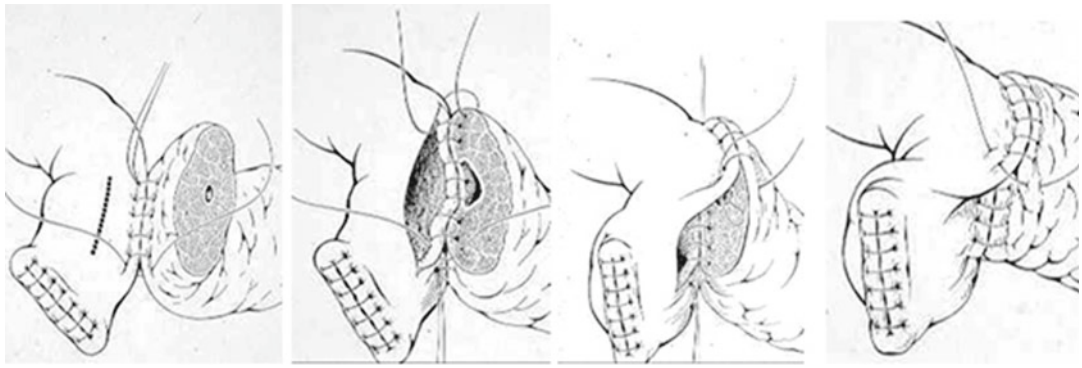

**Fig. 3.5** Scheme of the anastomosis technique showing the two layer suture of the posterior wall (*two left pictures*) and the anterior wall (*two right pictures*)

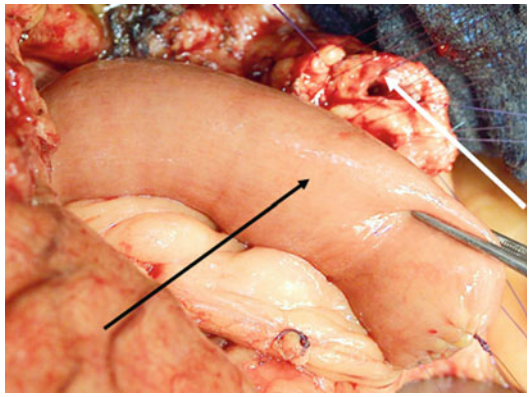

**Fig. 3.6** Intraoperative situs during pancreatico-jejunostomy. Prepared duct sutures (*white arrow*) and jejunal loop (*black arrow*)

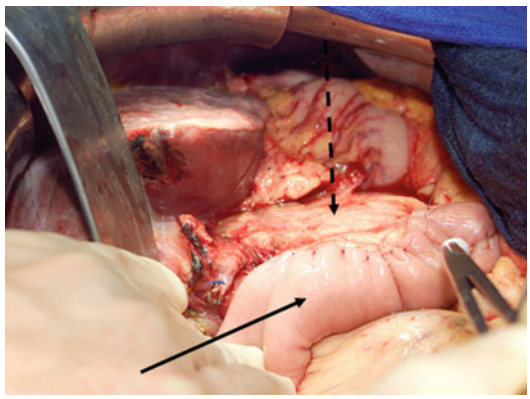

**Fig. 3.7** Intraoperative situs of the completed end-to-side pancreatico-jejunostomy. *Black arrow*: jejunal loop, *broken black arrow*: pancreatic remnant

48 h postoperatively, should be preceded by analysis of pancreatic enzyme levels in the drain fluid (Bassi et al. 2010).

The perioperative management includes perioperative, prophylactic antibiotics using mezlocillin (or ciprofloxacin in case of penicillin allergy) and metronidazole beginning before the operation, and repeated just once after 4 h. We do not use prophylactic, perioperative octreotide as a routine procedure unless the pancreas has a soft tissue texture intraoperatively. In these cases, octreotide is administered during the operation and continued for 5 days at a dosage of 200 μg 3 times/day. Because of good evidence from a recent metaanalysis (Gurusamy et al. 2010) that routine perioperative octreotide prophylaxis does not prevent pancreatic leakage, we believe that the use of octreotide should be restricted to individual situations and only if the surgeon classifies the pancreatic anastomosis as "high risk" due to soft tissue and a small diameter pancreatic duct.

A nasogastric tube is inserted at the beginning of the operation under general anesthesia and removed at the end of the operation. Oral intake of fluids is allowed beginning on the first postoperative day with progression to a more regular diet by about the fifth postoperative day.

For neoplasms of the body and tail of the pancreas, similar diagnostic measures are used as described above for pancreatic head neoplasms. We do not use diagnostic laparoscopy routinely and only when there is strong suspicion of tumor spread to the peritoneal cavity when there is a markedly increased serum CA 19-9 level without visible extrapancreatic spread or ascites on the CT. If there are no contraindications, distal pancreatectomy is performed by an open approach via a median or transverse laparotomy, depending on individual patient anatomy.

Distal pancreatectomy for oncologic indications always includes splenectomy to achieve a radical resection and a sufficient lymphadenectomy. After dissection of the superior mesenteric and portal mesenteric vein, the neck of the pancreas is transected. We prefer sharp transaction of the pancreatic neck for several reasons. First, the results of the recently completed DISPACT study (Diener et al. 2011) did not show any advantage of closure of the stump of the pancreatic remnant with a mechanical stapler, and second, the use of staplers may be contraindicated in thick or fibrotic glands. After dissection, bleeding is controlled by individual, non-resorbable atraumatic sutures (e.g. 5-0 Novafil). The pancreatic duct is cannulated, and if there is free passage toward the duodenum, the duct is closed selectively with a Z-shaped suture. The cut surface is then oversewn systematically using U- or Z-shaped sutures of slowly absorbable monofilament (e.g. 5-0 PDS). We do not use any synthetic patches for sealing of the pancreas. If possible, the falciform ligament is mobilized and transposed through the lesser omentum to serve as an autogenous tissue

**Results from Heidelberg 01/2006–12/2008**

| Parameter | Number | % |
|---|---|---|
| Patients | 537 | 100 |
| Pylorus-preserving pancreatoduodenectomy | 287 | 53.4 |
| Classic pancreatoduodenectomy (including antrectomy) | 40 | 7.4 |
| Total pancreatectomy | 82 | 15.3 |
| Distal pancreatectomy | 128 | 23.9 |
| 30-day mortality | 15 | 2.8 |
| Hospital stay (median, IQR) | 12 (10–17) | |
| Tumor stage (UICC) | | |
| 0 | 24 | 4.5 |
| I | 13 | 2.4 |
| II | 438 | 81.6 |
| III | 45 | 8.4 |
| IV | 17 | 3.1 |
| R0 | 194 | 36.1 |
| R1[a] | 327 | 60.9 |
| R2 | 16 | 3.0 |
| Morbidity | | |
| Postoperative bleeding | 34 | 6.3 |
| Pancreatic fistula (grades B and C) | 23 | 4.2 |
| DGE | 125 | 23.9 |
| Wound infection | 16 | 3.0 |

[a]According to Esposito et al. (2008)

patch and fixed with resorbable sutures on the posterior and anterior aspect of the cut surface of the pancreatic stump.

The lymphadenectomy during distal pancreatectomy includes the lymph nodes in the hepatoduodenal ligament, the celiac trunk, and the left side of the superior mesenteric artery. In addition, all fat and soft tissue on the anterior aspect of Gerota's fascia is removed en bloc with the specimen and the spleen. Usually 25–30 lymph nodes are included in the specimen for histopathologic evaluation. During the lymph node dissection of the hepatoduodenal ligament, a cholecystectomy is performed routinely.

At the end of the operation, two closed suction drains (12 mm, EasyFlow®) are placed routinely near the pancreatic stump and in the subdiaphragmatic space from the left side of the abdomen. Drain removal is preceded by analysis of pancreatic enzyme levels in the drain fluid and can usually be performed 72–96 h postoperatively.

The perioperative management of patients after distal pancreatectomy is similar to that after partial pancreatoduodenectomy in terms of perioperative, prophylactic antibiotics (mezlocillin or ciprofloxacin in case of penicillin allergy and metronidazole) and perioperative octreotide prophylaxis if the pancreas has a soft texture intraoperatively. The nasogastric tube inserted at the beginning of the operation is removed at the end of the operation. Oral intake of the patients is allowed on the first postoperative day with fluid, and the diet is advanced quickly.

For histopathologic evaluation of the pancreatic cancer specimen, the revised R1 classification is used in Heidelberg (Esposito et al. 2008). This staging includes an R1 classification whenever tumor cells are close to (<1 mm) or infiltrate the resection margin, which leads to a substantially greater proportion of R1 resections in our patient cohort due to a large number of specimens in which tumor cells do not infiltrate but are close to the margin. These resections would be classified as R0 resections in other institutions; however, we believe that the new R1 classification is more useful and accurate regarding prognostic implications and have implemented this standardized definition since 2005.

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