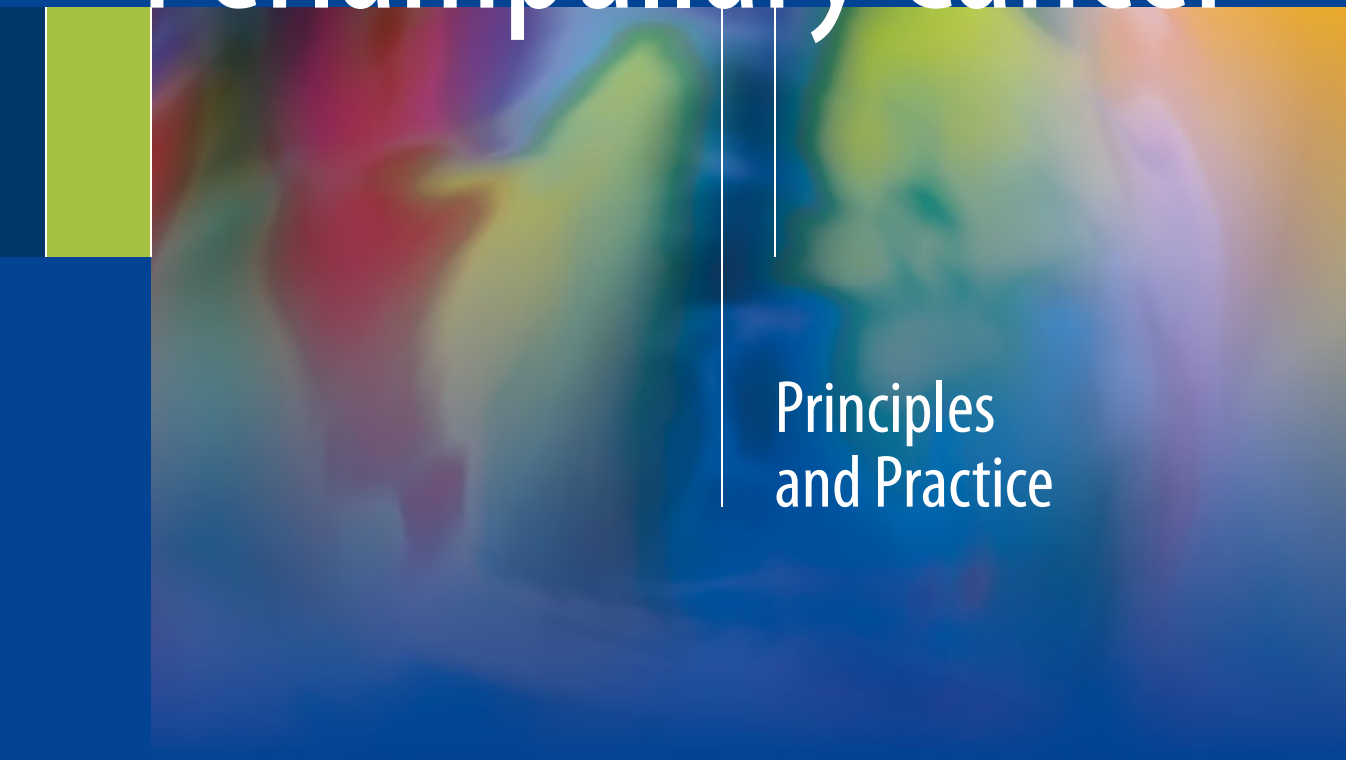
Mallika Tewari
Editor

Surgery for Pancreatic and Periampullary Cancer



Principles and Practice

Springer

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Foreword

Modern science and technologies have enabled clinicians in recent years to better understand perhaps the least understood of human organs—the pancreas. Greater awareness and increased detection of pancreatic pathologies have aroused interest among basic researchers, pancreatologists, gastroenterologists, and pancreatic surgeons. Despite phenomenal advances in unraveling the mystery of pancreatic and periampullary cancers, radical and high-quality surgery by experienced surgeons remains the only curative treatment option in these aggressive cancers.

Pancreatic surgery is widely regarded as the most challenging of surgeries. The reasons are easy to understand, viz., complex anatomical location with variations that are a norm rather than an exception and a reconstruction and difficult lymphadenectomy that are often the Achilles heel dictating short- and long-term outcomes. To add to the complexity, almost all pancreatic resections involve a steep and long learning curve with experience being accumulated only after many years of dedicated practice.

On this background, the book *Surgery for Pancreatic and Periampullary Cancer: Principles and Practice* by Dr. Mallika Tewari is timely. Every single chapter among 28 chapters is relevant as it takes the reader—right from the novice to the experienced pancreatic surgeon—through finer and more, importantly, technical aspects of diverse pancreatic resections. Evidence-based medicine guides (and often confuses) the interested surgeon about various age-old and yet controversial aspects of pancreatic surgery, and this book does well to bring into sharp focus the various pros and cons of technical aspects of pancreatic resections. The fact that the author list boasts of some of the finest names in pancreatic surgery lends credence to the firm belief that modern-day pancreatic resections should always be a blend of experience coupled with a keen desire for higher level of evidence. More recent developments in pancreatic resections have witnessed remarkable strides in vascular resections, multi-visceral resections, and minimally invasive laparoscopic and robotic pancreatic resections. The improvement in outcomes due to multidisciplinary care and emphasis on finer perioperative aspects such as nutrition and enhanced recovery after surgery further add to the excitement where the future is only expected to be brighter than ever before.

We have absolutely no doubt that this book by Dr. Tewari would serve as an excellent companion for anyone interested in pancreatic surgery for years to come.

June 2017

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Preface

The handbook *Surgery for Pancreatic and Periampullary Cancer: Principles and Practice* takes you on an academic journey exploring a difficult disease to treat, pancreatic and periampullary cancer. It is a useful read for all surgeons and surgical trainees involved in the management of pancreatic/periampullary cancer. This handbook gives minute details of various surgical techniques as practiced by experts themselves, who are world authorities on the subject. There are nine narrative chapters that are important practically from a surgeon's point of view and will help in the optimal management of the patients.

This handbook will provide an in-depth practical knowledge and means to understand the principles in carrying out difficult operations for pancreatic/periampullary cancer. It covers topics over a wide range of procedures and techniques, on both open and minimally invasive approach, in the form of "How I do it" chapters from reigning experts. The first five chapters on basic surgical anatomy, history, classification, imaging, and preoperative preparation are crisp and give the reader a good perspective and background before embarking on surgical techniques. The next 19 chapters, starting with the chapter on key steps of pancreaticoduodenectomy, detail various methods of pancreatic resection including venous and arterial resections and anastomotic techniques in a stepwise escalating manner. Also included are chapters on the upcoming laparoscopic and robotic approach. The last five chapters deal with postoperative complications, postoperative management, pathology reporting, and the importance of nutrition in patients undergoing such major surgical operations. The concluding chapter is on the novel technique of pancreas-preserving duodenectomy.

I was motivated to write a book on surgical techniques prevalent in pancreatic/periampullary cancer as I am fascinated by the challenges it offers. I have had the opportunity to visit some of the great institutes and hospitals across the world specializing in surgery for pancreatic cancer, and the energy, synergy, and dedication of the surgeons and their team were intoxicating. Numerous techniques, for example, of pancreatoenteric anastomosis are very intriguing, and concomitant vascular resections test the ultimate patience and expertise of the surgeon. I picked up many things, small and big, during my sojourn and wanted to compile them together in the form of a book so that this knowledge reaches out to all those committed in treating this cancer with the ultimate aim that the benefits of good meticulous surgery will actually translate in lower morbidities and quick postoperative recovery of our patients.

I feel very delighted and grateful to all my authors who accepted my request, even though I am a novice, and have written about the way they actually perform these complex operations supplemented with excellent illustrations and operative photographs. I thank Prof. Marcus Büchler, a doyen in the field, and Prof. S. Shrikhande for writing the Foreword. Last but not the least, I thank my mentors Prof. H. S. Shukla and Prof. Adarsh Chaudhary for all their kind help and motivation in completing this book.

Varanasi, Uttar Pradesh, India Mallika Tewari

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Mallika Tewari graduated from the Institute of Medical Sciences at Banaras Hindu University with distinction. Presently, she is Chief of the Hepato-Pancreatico-Biliary and Gastrointestinal Division and a Professor at the Department of Surgical Oncology, Institute of Medical Sciences. She has authored more than 100 peer-reviewed international and national publications.

She is the recipient of several prestigious international fellowships such as the UICC ICRETT, International Guest Scholarship of the American College of Surgeons, and European Society of Surgical Oncology traveling fellowship. She is an executive member of the World Federation of Surgical Oncology Societies (WFSOS) and Indian Association of Surgical Oncology (IASO). Further, Dr. Tewari is a reviewer for several international scientific journals and associate editor and editorial board member for the *Indian Journal of Surgery*.

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Surgical Anatomy of the Pancreas and the Periampullary Region

1

Keishi Sugimachi, Yuki Bekki, Tomohiro Iguchi, Masaru Morita, Yasushi Toh, and Kenji Takenaka

Abbreviations

AIPDV	Anterior inferior pancreaticoduodenal vein
ASPDA	Anterior superior pancreaticoduodenal artery
ASPDV	Anterior superior pancreaticoduodenal vein
GDA	Gastroduodenal artery
IPDA	Inferior pancreaticoduodenal artery
PIPDA	Posterior inferior pancreaticoduodenal artery
PLphI	Pancreatic head plexus I
PLphII	Pancreatic head plexus II
PSPDA	Posterior superior pancreaticoduodenal artery
PSPDV	Posterior superior pancreaticoduodenal vein
SMA	Superior mesenteric artery
SMA	Superior mesenteric vein

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1.1 General Anatomy of the Pancreas

The pancreas is a composite organ derived from dorsal and ventral buds that arise from either side of the distal foregut endoderm in embryonic development [1]. The pancreas lies transversely in the retroperitoneal sac with rotation of the duodenum. The duodenum is located on the right, the spleen on the left, and the stomach and the omental bursa above. The anterior surface of the pancreatic body and tail is overlapped by the peritoneum of the omental bursa.

The pancreas spreads in the mesoduodenum and is fixed to the retroperitoneum with various fused fasciae (Fig. 1.1) [2]. The anterior wall of the pancreatic head is covered by the mesoduodenum. The posterior wall of the mesoduodenum forms retropancreatic fusion fascia called the Treitz fascia with the posterior parietal peritoneum. The Treitz fusion fascia becomes the left Toldt fusion fascia at the body and tail of the pancreas, and the superior mesenteric artery (SMA) penetrates the fascia (Figs. 1.1 and 1.2). At the anterior surface of the pancreatic head, the transverse and ascending mesocolon forms fusion fascia with the mesoduodenum. This is continuous to the right Toldt fusion fascia, which is formed

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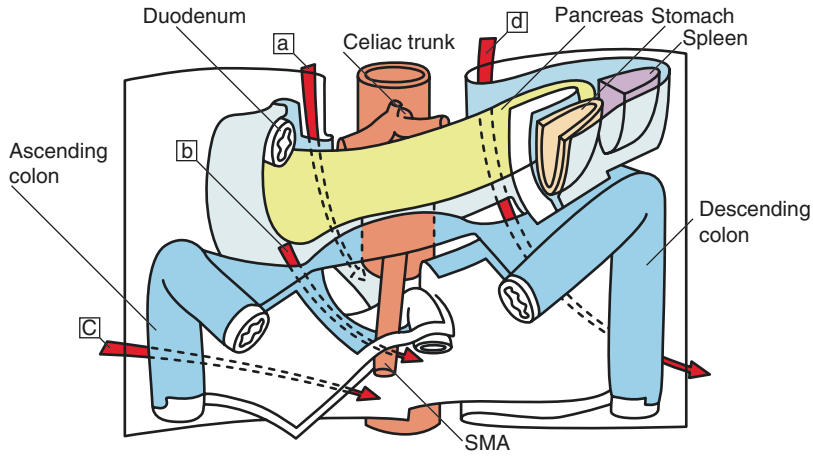

Fig. 1.1 Fused fasciae related to the pancreas. (**a**) The pancreatic head is covered by the mesoduodenum. The mesoduodenum and retroperitoneum form the Treitz fusion fascia. (**b**) The mesocolon (transverse colon) forms fusion fascia with the mesoduodenum. (**c**) The mesocolon (ascending colon) and parietal peritoneum form the right Toldt fusion fascia. (**d**) The left Toldt fusion fascia is formed by the retroperitoneum and peritoneum of the bursa omentalis. Modified from Perlemuter L et al: Cashiers d'Anatomie. Abdomen (I), 3rd ed, Masson & Cie, Paris, 1975

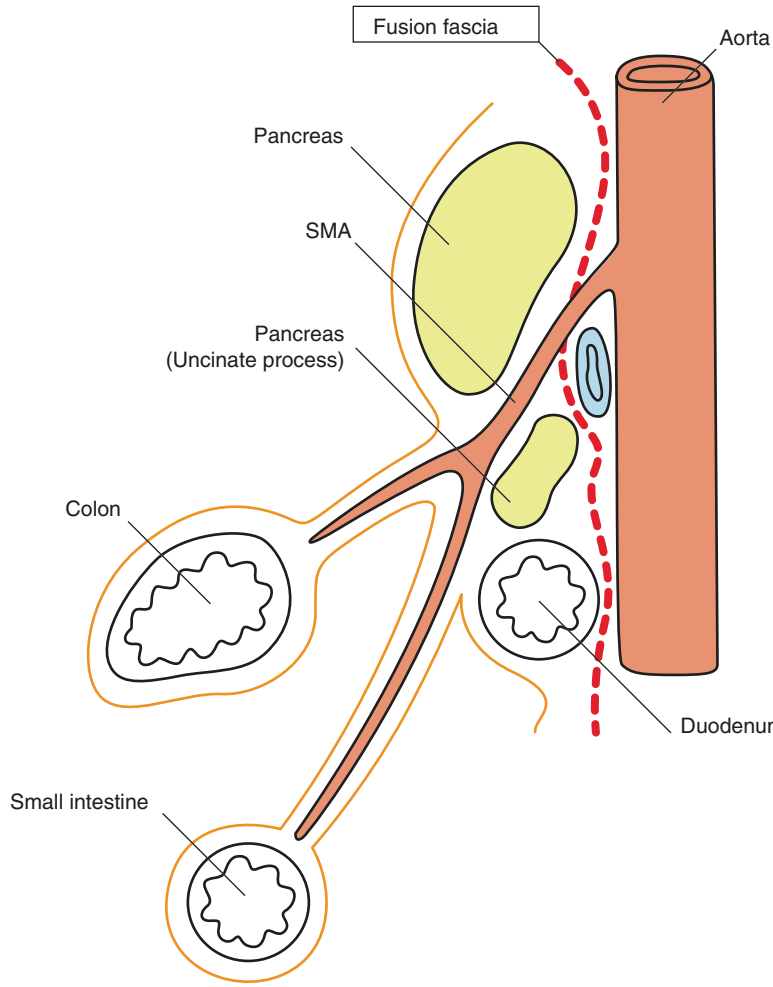

Fig. 1.2 The retroperitoneal fusion fascia of the pancreas. The pancreas and the duodenum rotate and attach to the retroperitoneum forming fusion fascia, and the superior mesenteric artery penetrates the fascia. Left renal vein locates between aorta and fusion fascia (*light blue*). Modified from Skandalakis, JE et al: The Pancreas, vol 1, Blackwell Science, London, 1998

by the ascending mesocolon and parietal peritoneum. Posteriorly, the pancreatic bed in the retroperitoneal space contains the hilum of the right kidney, the inferior vena cava, the aorta, the left kidney, and the hilum of the spleen, from right to left (Fig. 1.2). Pancreaticoduodenal arteries and veins are present between pancreatic parenchyma and fused fasciae. Therefore, these fasciae have to be dissected for pancreatectomy.

1.2 Arteries

The celiac trunk and SMA provide the arterial supply to the pancreas. Variations are common, but for the most part, the body and tail are supplied by branches of the splenic artery. However, the pancreatic head and uncinate process receive arterial supply through arcades originating from the gastroduodenal artery (GDA) and the first branch of the SMA (Fig. 1.3).

The GDA, the branch of the common hepatic artery, ramifies the posterior superior pancreaticoduodenal artery (PSPDA) at the superior edge of the pancreas and becomes the anterior superior pancreaticoduodenal artery (ASPDA). The ASPDA runs along the anterior surface of the pancreas and branches to the right gastroepiploic artery at the site of the pyloric ring. The PSPDA runs above the common bile duct from left to right and travels down the posterior surface of the pancreas. The PSPDA supplies the papilla of Vater and finally forms an arcade with the posterior inferior pancreaticoduodenal artery (PIPDA). The arcade of the PSPDA and PIPDA forms a spiral formation around the lower common bile duct in an anti-clockwise manner (Fig. 1.3) [3].

The right and left hepatic arteries usually arise from the celiac trunk and common hepatic artery. However, there are common variations where the right hepatic artery or common hepatic artery originates from the SMA (Fig. 1.4). A replaced left hepatic artery originates from the left gastric artery. A replaced right hepatic artery arising from the SMA is commonly observed, but a replaced common hepatic artery is relatively rare. This replaced right hepatic artery is the artery that needs to be preserved during pancreaticoduodenectomy to preserve hepatic arterial flow. However, this artery usually runs behind the pancreatic head

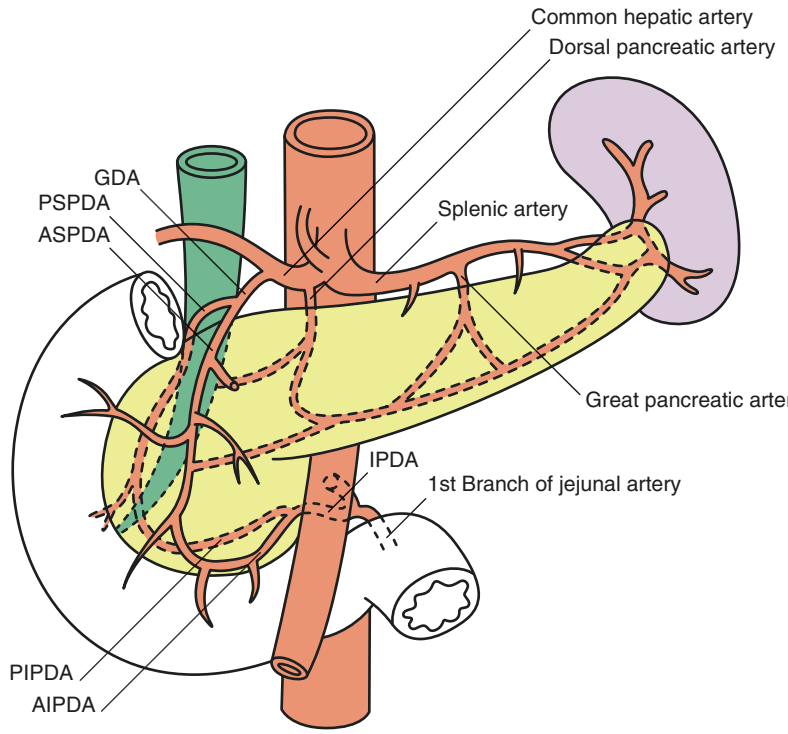

Fig. 1.3 Arterial supply of the pancreas. The pancreas has a rich arterial supply that is derived from the celiac trunk and superior mesenteric artery. The superior and inferior pancreaticoduodenal arteries form arcades and supply the pancreatic head. The dorsal pancreatic artery descends posterior to the pancreas and supplies the pancreatic body and tail. Modified from Netter FH: Atlas of Human Anatomy, 3rd ed. Icon Learning Systems, New Jersey, 2004

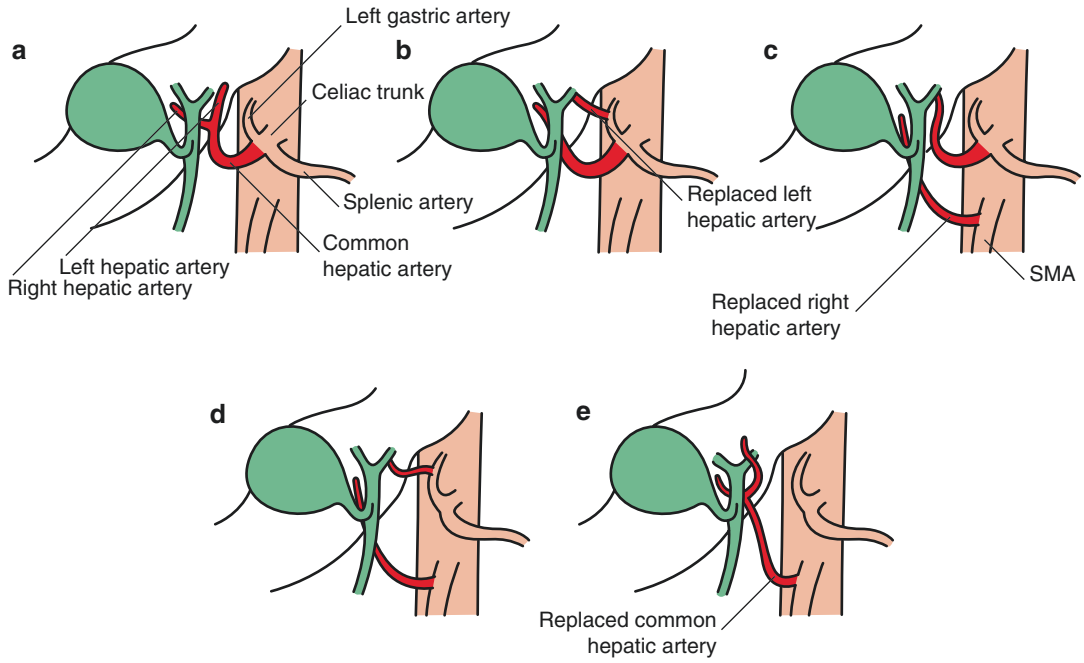

Fig. 1.4 Variants of the hepatic artery. A replaced hepatic artery is a vessel that does not originate from the proper hepatic artery and provides sole supply to the liver. A replaced right hepatic artery originating from the superior mesenteric artery or a replaced left hepatic artery from the left gastric artery is commonly observed. A replaced common hepatic artery is relatively rare. (**a**) no replaced hepatic artery, (**b**) replaced right hepatic artery, (**c**) replaced left hepatic artery, (**d**) replaced right and left hepatic arteries, (**e**) replaced common hepatic artery. Modified from Gray's Anatomy. 4th ed. Standring S. ed, Churchill Livingston, Elsevier, 2008

and is thus easily invaded by adenocarcinoma of the pancreas. Avoiding injury of the right hepatic artery when the extrahepatic bile duct is divided is also important. The right hepatic artery usually runs transversely from left to right behind the bile duct, in front of the portal vein. A replaced right hepatic artery ascends behind the portal vein and bile duct and can be identified by pulsation behind the portal vein. A replaced left hepatic artery from the left gastric artery lies in the upper portion of the lesser omentum and thus may be injured during mobilization of the stomach.

The inferior pancreaticoduodenal artery (IPDA) branches from the posterior side of the SMA and forms a common trunk with the first branch of the jejunal artery. The IPDA then branches into the anterior IPDA and posterior IPDA (Fig. 1.5) [4]. In pancreaticoduodenectomy, pancreaticoduodenal branches from the SMA must be identified and divided to resect the pancreas and duodenum. The common branch of the IPDA and the first branch of the jejunal artery usually arise from the SMA. However, in some cases, the IPDA and the first branch of the jejunal artery independently arise from the SMA (Fig. 1.5). In addition to the main IPDA, the pancreatic head and duodenum are usually supplied from minor branches from the proximal SMA. The IPDA possibly arises from a replaced hepatic artery, which is a branch of the SMA (Figs. 1.4 and 1.5). Identifying and preserving a replaced hepatic artery are important, while the IPDA has to be sacrificed during surgery. Dissecting the IPDA at the first stage of pancreaticoduodenectomy prevents congestion of the pancreatic head and duodenum and thus may result in less blood loss during surgery [5].

When the pancreatic parenchyma at the pancreatic neck above the superior mesenteric vein (SMV) is divided, two arteries at the cranial and

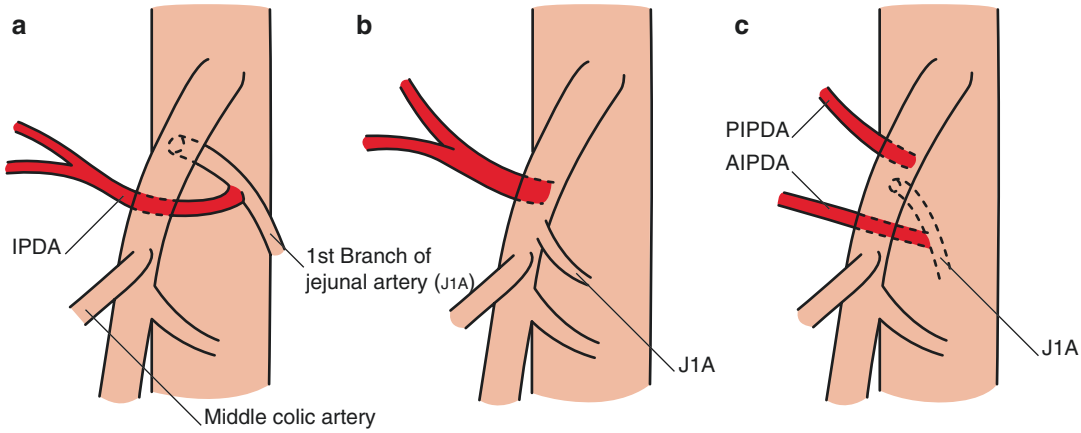

Fig. 1.5 Variation of the inferior pancreaticoduodenal artery. Typically, the inferior pancreaticoduodenal artery (IPDA) and the first branch of the jejunal artery form a common trunk. In minor variations, the IPDA directly arises from the superior mesenteric artery, or the anterior and inferior IPDAs independently arise from the SMA and the first branch of the jejunal artery. (**a**) common trunk of IPDA and J1A arises from SMA (major variation), (**b**) IPDA directly arised from SMA, (**c**) PIPDA and AIPDA independently arise from SMA

caudal sides of the pancreas are usually seen. The dorsal pancreatic artery arises from the splenic artery, the celiac trunk, or the common hepatic artery. The dorsal pancreatic artery then travels down the posterior surface of the pancreas and forms an arcade with the branch from the GDA (suprapancreatic branch). The inferior pancreatic artery branches from the ASPDA and runs transversely and forms an arcade with the dorsal pancreatic artery or the great pancreatic artery (peripancreatic arcade).

1.3 Portal Vein

Venous drainage from the pancreas goes to the splenic vein, SMV, and portal vein. The posterior superior pancreaticoduodenal vein (PSPDV) runs along the PSPDA at the posterior surface of the pancreatic head and drains into the portal vein. The anterior superior pancreaticoduodenal vein (ASPDV) collects venous drainage from the anterior surface of the pancreas and the duodenum. The superior right colic vein, the right gastroepiploic vein, and the ASPDV form the common venous trunk called the gastrocolic trunk of Henle, which drains into the SMV (Fig. 1.6).

Pancreatic adenocarcinoma often invades the portal vein and its branches, thus requiring combined resection and reconstruction of the portal vein or SMV. In the NCCN Guidelines, contact with the most proximal draining jejunal branch into the SMV is classified as unresectable pancreatic adenocarcinoma [6]. Usually the first jejunal branch of the SMV branches from the posterior surface of the SMV, merges with the anterior inferior pancreaticoduodenal vein (AIPDV), and runs transversely from right to left behind the SMA. There is a minor variation where the first jejunal branch of the SMV arises from the surface of the left side of the SMV and runs from right to left in front of the SMA (Fig. 1.7). The inferior mesenteric vein drains into the splenic vein, SMV, or the confluence of the splenic vein and SMV (Fig. 1.8).

The draining veins of the pancreatic body and tail go to the splenic vein or to the SMV. The left gastric vein drains into the splenic vein or the portal vein. The anatomy of the portal vein and its branches for portal vein resection and reconstruction should be evaluated preoperatively. The inferior mesenteric vein and left gastric vein might be drainage vessels of the remnant pancreas and the spleen when portal vein resection without splenic vein reconstruction is planned.

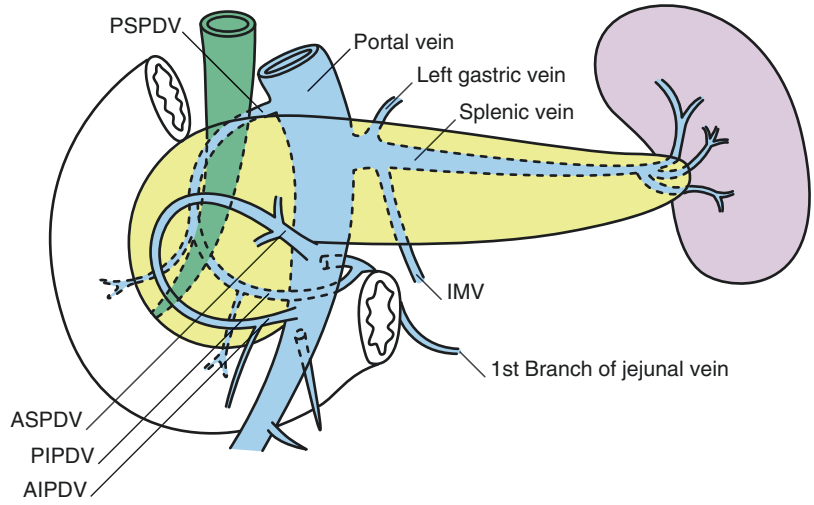

Fig. 1.6 Venous drainage system of the pancreas. The venous system of the pancreas primarily travels into the portal vein. The head drains into the superior and inferior pancreaticoduodenal veins. The body and tail drain via small veins that run directly into the splenic vein. Modified from Netter FH: Atlas of Human Anatomy, 3rd ed. Icon Learning Systems, New Jersey, 2004

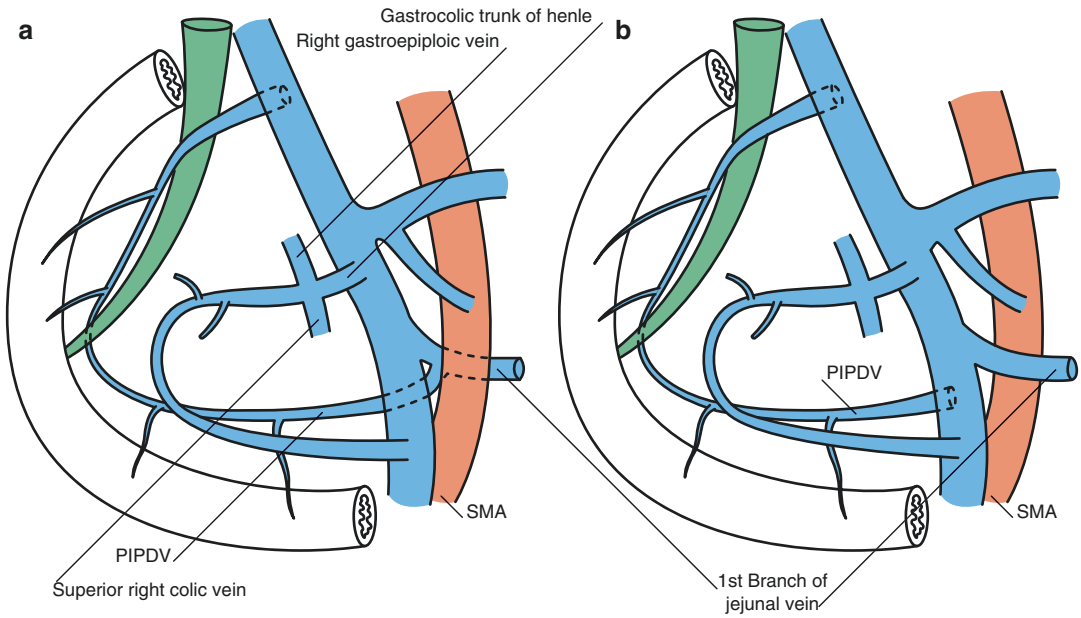

Fig. 1.7 Venous drainage of the pancreatic head and variations of the inferior pancreaticoduodenal vein. The first branch of the jejunal vein runs behind the superior mesenteric artery (SMA), anastomoses the posterior inferior pancreaticoduodenal vein (PIPDV), and drains into the posterior surface of the superior mesenteric vein (SMV). In a minor variation, the first branch of the jejunal vein runs in front of the SMA and drains into the left surface of the SMV, and the PIPDV solely drains into the SMV. (**a**) jejunal vein runs behind SMA, (**b**) jejunal vein runs in front of SMA (minor variation)

1.4 Pancreatic Ducts

The main pancreatic duct, the duct of Wirsung, arises in the tail of the pancreas and runs through the pancreatic parenchyma. The duct of Wirsung terminates at the papilla of Vater in the duodenum with the common bile duct in Oddi's sphincter muscle (Fig. 1.9). The minor or accessory

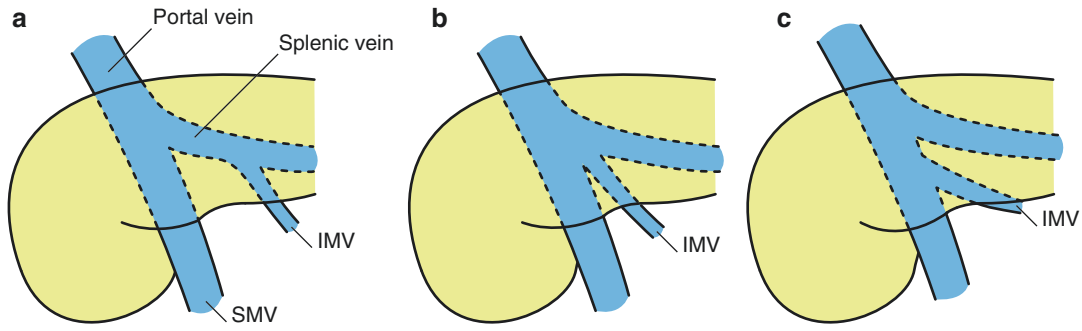

Fig. 1.8 Variation of the merging confluence of the inferior mesenteric vein. (**a**) The inferior mesenteric vein drains into the splenic vein, the superior mesenteric vein, or (**b**) the confluence of the splenic vein and (**c**) the superior mesenteric vein. Modified from Kimura W. Surgical anatomy of the pancreas for limited resection. J Hepatobiliary Pancreat Surg, 2000

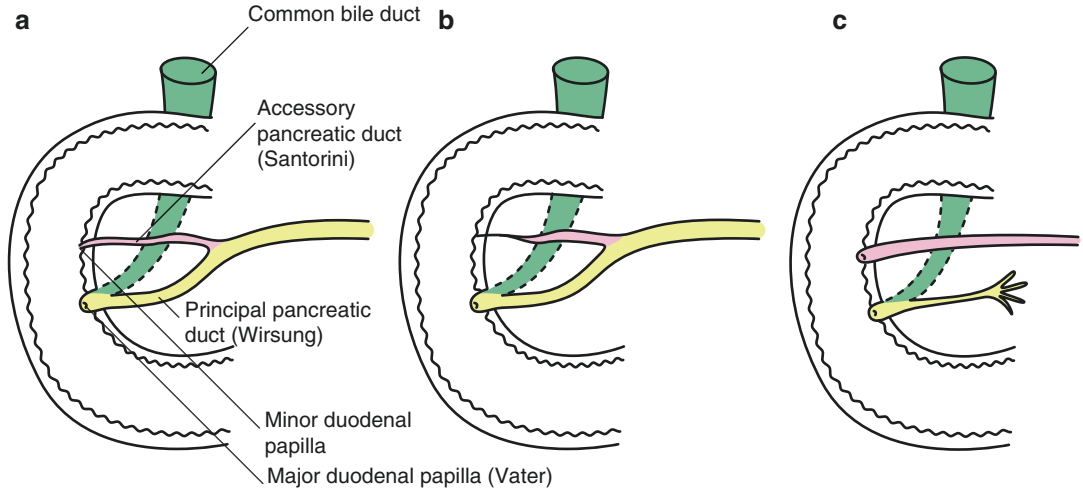

Fig. 1.9 Variations of the pancreatic ducts. (**a**) The ducts of Wirsung and Santorini open into the duodenum. (**b**) The duct of Santorini ends blindly in the duodenal wall. (**c**) The duct of Wirsung is smaller than the duct of Santorini and these ducts are not connected. The duct of Santorini carries the entire secretion (pancreatic divisum). Modified from Skandalakis LJ et al. Surgical embryology and anatomy of the pancreas. Surg Clin North Am, 1993

pancreatic duct, the duct of Santorini, is smaller than the main duct. The duct of Santorini extends from the main duct to enter the duodenum at the lesser papilla. This papilla usually lies approximately 1–2 cm proximal and slightly anterior to the major papilla. The duct of Wirsung belongs to the ventral pancreas, and the duct of Santorini does the dorsal pancreas in development. The accessory pancreatic duct drains the uncinate process and inferior part of the head of the pancreas. Several variations are encountered because of the developmental origin of the two pancreatic ducts. The accessory pancreatic duct usually communicates with the main duct and both ducts open into the duodenum. There is another variation where the end of the accessory duct is closed and not open to the duodenum. In some cases, the main pancreatic duct is smaller than the accessory pancreatic duct, and the two are not connected. In those cases, the accessory duct carries most of the pancreatic juice (pancreatic divisum) (Fig. 1.9).

1.5 Duodenal Papilla

The duodenal papilla (the papilla of Vater) lies at the end of the intramural portion of the common bile duct. There is a complex of sphincter musculature that is composed of circular or spiral smooth muscle fibers surrounding the intramural portion of the common bile and pancreatic ducts (Fig. 1.10). A duodenal diverticulum lying close to the papilla may be present, and the papilla has been found in a diverticulum. The pancreatic duct and the common bile duct usually merge in the duodenal wall, and this is covered by the sphincter of ampulla and opens in the duodenal papilla (Fig. 1.10). There is a variation where the pancreatic and common bile ducts open into the duodenum at separate points. In some cases, the main pancreatic duct and the common bile duct merge outside of the duodenal wall, and the conjunct duct is covered by sphincter musculature (pancreaticobiliary maljunction) (Fig. 1.10). In these cases, pancreatobiliary juice reflux possibly causes biliary inflammation and malignancy [7].

1.6 Nerves

The pancreas is innervated by the sympathetic (the greater and lesser splanchnic nerves) and the parasympathetic (vagus nerve) nervous systems. These nerve fibers collect and form the celiac ganglia. Nerve fibers from the right and left celiac ganglia merge at the root of the celiac trunk and SMA and form the celiac plexus. The plexus originates from the celiac-superior mesenteric plexus and directly reaches the pancreatic head or uncinate process. There are no identical nerve plexuses at the pancreatic body and tail. According to the General Rules for the Study of Pancreatic Cancer by the Japan Pancreas Society, the plexus behind the pancreatic head can be differentiated into two parts (Fig. 1.11). The region that mainly includes nerve tissue that is distributed to the dorsal surface of pancreatic head and the cranial edge of the uncinate process from the right of the celiac ganglia is named the pancreatic head plexus I (PLphI). The wide plexus that is distributed to the uncinate process from the superior mesenteric ganglia is called the pancreatic head plexus II

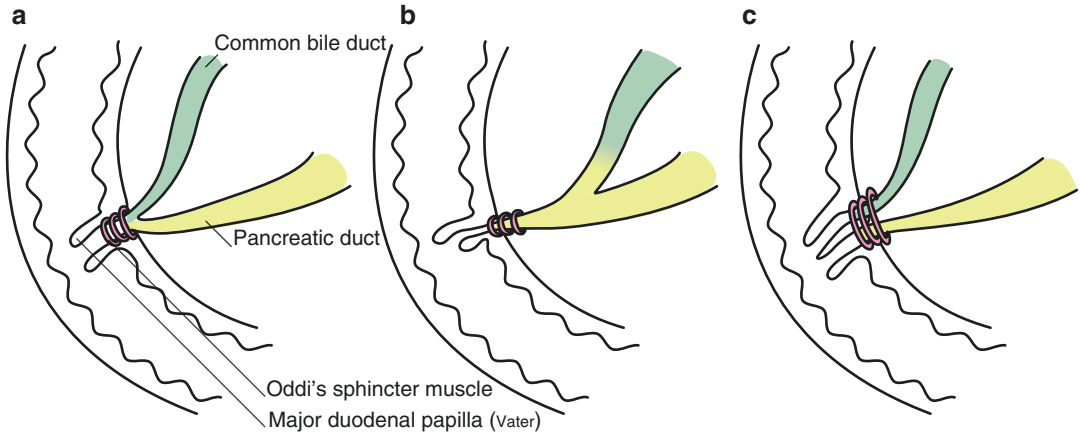

Fig. 1.10 Diagram of the relations of the pancreatic and common bile ducts. (**a**) In normal anatomy, the ampulla is the common pancreaticobiliary channel below the junction of the ducts within the papilla. The pancreatic duct opens into the common bile duct at a variable distance from the orifice of the major duodenal papilla. (**b**) The pancreatic duct anastomoses the common bile duct outside of the duodenal wall, and thus there is a long conjunct duct. In this case, pancreatic juice refluxes into the bile duct (pancreaticobiliary maljunction). (**c**) The pancreatic and common bile ducts open separately on the major duodenal papilla

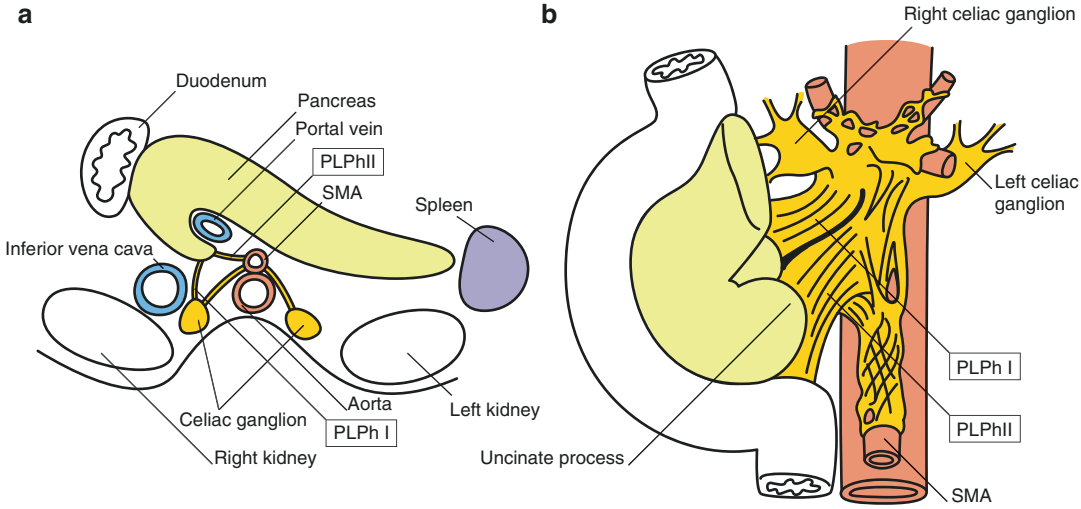

Fig. 1.11 The plexus of the pancreatic head. The pancreatic head plexus I extends to the dorsal surface of the pancreatic head and the cranial edge of the uncinate process from the right of the celiac ganglia. The pancreatic head plexus II is a wide plexus that extends to the uncinate process from the superior mesenteric ganglia. (**a**) a schematic diagram of pancreatic plexsus from cross section, (**b**) plexsus of pancreatic head and arteries. Modified from Japan Pancreas Society: The General Rules for the Study of Pancreatic Cancer. 6th ed. Kanehara, Tokyo, Japan 2013

(PLphII) (Fig. 1.11). The PLphII includes the IPDA and is continuous to the plexus of the mesojejunum. There is usually no clear septum or space between the PLphI and PLphII. Para-SMA lymph nodes are present at the ventral and dorsal sides of the plexus. In pancreaticoduodenectomy, the pancreatic head and SMA have to be removed by dissecting these pancreatic plexuses.

Areolar tissue surrounding the PLphII is considered to be anatomically consistent with the "mesopancreas" [8]. However, the concept and nomenclature of the mesopancreas is unclear and controversial. Some authors consider that the mesopancreas cannot be called a true mesentery because it does not have a fascial envelope attaching the pancreas to the posterior wall of the abdomen. Additionally, the mesopancreas does not contain all of its blood vessels and all its primary draining lymphatics and lymph nodes of the pancreas [9]. The mesopancreas or PLphII consists of not only nerve fibers but fibrous tissue, fat, lymphatics, and minor vessels.

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2 Overview of Resections for Pancreatic and Periampullary Cancer

June S. Peng and Gareth Morris-Stiff

2.1 Early Pancreatic Surgery

Surgery of the pancreas was made feasible in the 1800s with the rise of anesthesia and acceptance of antisepsis. The earliest reports involved management of pancreatic cysts through drainage and marsupialization [1].

The first intentional resections of the pancreas involved the pancreatic tail, as it was perceived to be less complex due to simpler anatomy, fewer adjacent vascular structures, and lack of need for complex reconstruction. Friedrich Trendelenburg [FIG] is widely credited with performing the first distal pancreatectomy and splenectomy in 1882 (Bonn, Germany) for a large retroperitoneal mass which pathology revealed to be a spindle cell sarcoma. The patient suffered from a wound infection and malnutrition and expired a few weeks after surgery. Early experience with distal pancreatic resection was sparse, with 24 surgeries performed by 21 surgeons between 1882 and 1905, with a mortality rate of 53% [2–4].

2.2 Pancreatic Head Resections

Despite the perceived challenges of proximal pancreatic resections, the first pancreatic head and partial duodenal resection was performed by Alessandro Codivilla [FIG] in February 1898 (Imola, Italy), published after the fact by his successor Bartolo dal Monte [5]. Codivilla at that stage of his career was interested in abdominal operations and had experience performing gastric surgeries, although he would later shift to orthopedic surgery. The patient was explored for epigastric distension and vomiting and found to have a tumor involving the distal stomach and pancreatic head. The operation necessitated resection of the distal stomach, portion of the duodenum, pancreatic head, and distal common bile duct (CBD). Reconstruction was performed with a Roux-en-Y gastrojejunostomy and cholecystojejunostomy [FIG]. The pancreatic stump was likely closed [5, Codvilla]. Pathology revealed a pancreatic cancer, and postoperatively, the patient appeared to develop a pancreatic fistula that drained via the incision. Unfortunately, the patient developed steatorrhea, hyperglycemia, and malnutrition and expired approximately 3 weeks after the operation. Although the extent of this operation was not anatomic by today's standards and was not reported to the surgical community at the time, it remains an important landmark in the history of pancreatic surgery.

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In the same year in the United States, William Halsted [FIG] performed the first transduodenal ampullary resection in 1898 (Baltimore, Maryland) for presumed choledocholithiasis but found to be a periampullary cancer intraoperatively [6, 7]. This cancer was excised locally with reimplantation of the pancreatic duct and CBD into the duodenum. The patient required re-exploration for recurrent jaundice. Halsted was unable to pass a probe from the CBD to the duodenum and performed a cholecystoduodenostomy. The patient expired several months later with recurrent jaundice and autopsy confirmed recurrent cancer.

Early experience of periampullary excision also yielded poor outcomes with an operative mortality ranging from 30 to 70% of the 109 cases reported through 1941 [1, 8]. The management of the pancreatic duct, and usage of additional biliary drainage, was variable in this series. Overall mortality of transduodenal periampullary excisions was 29.0%, with marked improvements over time, from 43.3% prior to 1925 to 14.9% subsequent to 1925. The cumulative series also included 15 patients who underwent resection of the duodenum and pancreatic head, with a mortality of 26.6%.

The management of the pancreatic remnant provided a perplexing problem in the early era of pancreatic resections. A handful of reports described traumatic disruption and resections, where the pancreatic capsule was approximated but almost all were complicated by leaks which were anticipated and drained prophylactically [1]. Laboratory work in human cadavers by Abel Desjardins in 1907 (Paris, France) [1] and canine model by Robert Coffey in 1909 (Portland, Oregon) [9] would inform later work in live humans. Coffey noted that "the pancreas remains technically almost a stranger to the surgeon" and performed pancreatoduodenectomy (PD) in a dog model which included partial pancreatic resection with reconstruction using a two-layer invaginating pancreaticojejunostomy (PJ), choledochoduodenostomy, and loop gastrojejunostomy (GJ) [FIG].

A number of surgeons subsequently made forays into pancreatic resections. Oskar Ehrhardt in 1907 (Konigsberg, Prussia) performed a gastrojejunostomy for a patient with gastric outlet obstruction related to a pancreatic tumor [1]. When the patient developed recurrent obstruction, Ehrhardt performed a distal gastrectomy, duodenectomy of the second portion, and partial pancreatic head resection without re-approximation of the capsule. The patient had a pancreatic leak and died 5 months later of recurrent cancer.

The first successful PD was performed in two stages by Walther Kausch in 1909 (Berlin, Germany). The preference for a two-stage operation was due to the need for biliary-enteric bypass to resolve jaundice, malnutrition, and impaired coagulation in patients with long-standing jaundice, which resulted in malnutrition and coagulopathy. The first stage included a loop cholecystojejunostomy with a Braun anastomosis [FIG], and the second stage was performed 2 months later, with resection of the distal stomach, proximal duodenum, distal CBD, and portion of the pancreatic head [1, 3]. Kausch performed the reconstruction with a pancreaticoduodenostomy in two layers, closure of the CBD and a retrocolic loop gastrojejunostomy [FIG]. Pathology revealed a pancreatic adenocarcinoma. The patient developed a leak postoperatively which resolved spontaneously but subsequently died of cholangitis 9 months later.

The first successful one-stage non-anatomic PD was performed by Georg Hirschel [FIG] in 1912 (Heidelberg, Germany) for an ampullary carcinoma. The resection included portions of the duodenum, head of the pancreas, and distal CBD [6]. Reconstruction was performed with a pancreaticoduodenostomy, posterior GJ, and drainage of the CBD into the "lower duodenum by means of a rubber tube" [6, 10]. The patient died 1 year later of unclear reasons.

Ottorino Tenani in 1922 (Florence, Italy) performed a two-stage operation, similar to Whipple's initial case over a decade later. The first stage included a posterior GJ and ligation of the distal CBD, and a choledochoduodenostomy was performed. A month later, the duodenum and head of the pancreas were resected, and "the stump of the pancreatic head was implanted into the lower end of the transected duodenum" [10].

The performance of a choledochoduodenostomy by Tenani was the first, as well as the utilization of perioperative blood transfusion and postoperative enzyme replacement [11]. In total, seven partial PDs were performed by early surgeons in the era prior to Allen Whipple, with an operative mortality of 43% [1].

Allen Whipple performed his first PD in 1934 (New York City, New York). He is well known as the namesake of both the Whipple operation and Whipple's triad. He continued the work of his predecessors and was critical in transitioning the operation from the hands of the rare few into the mainstream. His work came at a critical historical time and was enabled by the experience and errors of others before him, as well as medical advances including vitamin K and blood storage and transfusions [10]. Whipple recognized the challenges of pancreatic surgery, the destructive nature of pancreatic enzymes, and the disease process itself which rendered patients jaundiced, malnourished, and prone to coagulopathy [12]. He summarized a total of 65 cases reported previously, which included 60 one-stage operations for periampullary lesions with a 38% mortality rate and 5 two-stage operations with a 16.6% mortality rate. The operative principles outlined by Whipple included a two-stage operation in order to optimize the patient. The first stage was a bypass procedure with a posterior loop gastroenterostomy, CBD ligation, and an anterior cholecystogastrostomy [FIG]. The second stage was performed 3–4 weeks later with vascular ligation of the GDA and pancreaticoduodenal arteries, resection of the second and third portions of the duodenum, partial pancreatic head resection, ligation of the ducts of Wirsung and Santorini with closure of the pancreatic capsule, and drain placement [FIG]. Whipple's first pancreaticoduodenostomy patient unfortunately died 30 hours after the second stage of operation. In a latter reflection, Whipple attributed the death to "duodenal leak with a diffusing peritonitis" presumably due to leak from the pancreaticoduodenal anastomosis [10, 13]. The three patients presented in the original 1935 series set the basis for resections of the periampullary region. Whipple highlighted the need for en bloc resection of the tumor with a margin, the benefits of a two-stage operation in order to resolve jaundice and improve nutrition, and he made a case for occlusion of the pancreatic duct, noting that the two surviving patient had relatively normal fat absorption and weight gain. His technique evolved from there, including the use of silk suture and omission of a pancreatico-enteric anastomosis for several years. Over the following years, he made several adjustments and changes based on the complications experienced. He avoided performing cholecystogastrostomy due to ascending cholangitis in his second and third patients and used a Roux-en-Y cholecystojejunostomy instead [14].

The first one-stage operation performed by Whipple was in March 1940 [10, 15]. The patient underwent exploration for a diagnosis of distal gastric carcinoma, but after transection of the mid-stomach, the mass was noted to be in the head of the pancreas. Whipple proceeded with pancreatoduodenectomy given the patient did not have jaundice and thus was not coagulopathic. Reconstruction was performed with an end-to-side GJ and end-to-end choledochojejunostomy in a loop fashion and closure of the pancreatic stump [14, 15]. The pathology revealed a nonfunctioning islet cell tumor. The patient was diagnosed with liver metastases 4 years later and survived 9 years after the initial operation. Subsequently, Whipple's preference was to perform a distal gastrectomy and complete duodenectomy with resection of the head of the pancreas. Reconstruction was performed by pulling up the jejunum through the mesocolic defect, with an end-to-end choledochojejunostomy, a two-layered PJ, and an end-to-side GJ [FIG from 1946 paper].

After initially abandoning a PJ anastomosis, Whipple noted that a large number of patients developed fistulae following pancreatic stump closure [10]. In 1942, he again constructed a PJ using a duct-to-mucosa inner layer and an outer layer for invagination. By 1945, he advocated a one-stage surgery, pancreaticojejunostomy rather than occlusion, with the use of an internal stent, and choledochojejunostomy rather than cholecystogastrostomy [6, 13].

In later reflections of his work, Whipple attributes progress in pancreatic surgery to vitamin K, blood transfusion, and "other shock prevention therapy" and the use of "silk technique" [13]. Although his case series was relatively small with an operative mortality rate of 33% that well exceeds modern standards [11], he paved the way for those to follow. Perhaps his most important contribution was that he "aroused a wave of optimism among surgeons which led to an aggressive application of this operation" to overcome the "wave of pessimism of such proportion that it appeared for a while that the operation … would abandoned entirely" [16].

Shortly after Whipple's first one-stage PD, Ridgeway Trimble in 1940 performed a one-stage PD (Baltimore, Maryland). His rationale for one rather than two stages was that "all the work is done in a clean operative field as opposed to a field masked and obscured by trauma of a preliminary operation" and because it was possible "to avoid injury to these structures and to effect the delicate restorative anastomoses" with "proper vitamin therapy and … transfusion at the very beginning of the operation" [17]. The patient underwent operative exploration for jaundice and abdominal pain and found to have an ampullary mass. An en bloc resection was performed on the pylorus, duodenum, and head of pancreas. The pancreatic stump was closed. A choledochojejunostomy was created 20 cm distal to the GJ. The patient recovered well postoperatively except for one episode of hemorrhage managed with a blood transfusion and had no long-term nutritional deficiencies related to the ligation of the pancreatic duct.

The one-stage PD became increasingly common as experience increased, with variations that brought the operation closer to the modern iteration. Verne Hunt in 1940 (Los Angeles, California) performed a one-stage PD for a patient with painless jaundice due to an ampullary cancer [8]. Hunt resected 3 in. of the second and third portions of the duodenum, distal CBD, and head of the pancreas. The pancreatic duct was ligated, and the cut parenchymal edge was closed with an omental patch. Reconstruction was performed with a posterior GJ, cholecystogastrostomy, and a T-tube was placed in the CBD. The patient developed a pancreatic fistula and bilious fluid that drained via the incision, both resolved with packing and wound care. She subsequently recovered well and was alive without recurrence at 1 year.

Hunt subsequently performed in 1941 another resection for ampullary carcinoma, this time including a total duodenectomy with resection of a portion of the pancreatic head. Reconstruction was performed by pulling the jejunum up through the mesocolic defect, and in addition he performed a pancreaticojejunostomy and choledochojejunostomy and a distal DJ [FIG].

Warren Cole and John Reynolds reported a series of five PDs in 1944 (Chicago, Illinois) [18]. Three were performed in one stage, and two were performed in two stages. The authors stressed starting the operation with an evaluation for metastatic disease, followed by kocherization of the duodenum and evaluation of venous involvement. They proceed with ligation of the gastroduodenal artery (GDA) and inferior pancreaticoduodenal artery. Four cases were performed with antrectomy, while one was pylorus preserving. In their variation, the distal duodenum or jejunum was oversewn and left in situ, a distal loop of the jejunum was brought into the right upper quadrant for reconstruction of the choledochojejunostomy most proximally, and an end-to-side GJ distal to that, with the pancreatic stump being closed. Reconstruction for the five cases varied, with three undergoing a loop GJ distal to the biliary anastomosis and two using Roux-en-Y configuration. Similar to Hunt and Child, they intentionally created the GJ distal to the biliary anastomosis, with the intention of avoiding cholangitis. Two patients developed persistent pancreatic fistulae, and there was one postoperative death. The authors also summarized the reconstructions utilized by other authors around the same time [FIG].

Many of the early PDs were non-anatomic due to concerns that the duodenum itself and pancreatic secretions were essential for life [14]. The first anatomic PD was performed in two stages by Alexander Brunschwig in 1937 (Chicago, Illinois) [19]. The first operation was a posterior

loop GJ, a cholecystojejunostomy distal to the GJ, and a Braun jejunojejunostomy. The second stage was performed a few weeks later with resection of the entire duodenum and pancreatic transection at the neck over the superior mesenteric vein (SMV), with ligation of the pancreatic stump. The CBD was ligated, and no further reconstruction was required as the patient had undergone enteric and biliary bypass during the first operation. Pathology revealed pancreatic cancer. The patient developed an enteric leak, which was controlled with a drain placed into the prior drain site. The patient spent almost 3 months in the hospital and developed recurrent jaundice before he expired. Autopsy revealed carcinomatosis and ascites and confirmed a distal duodenal stump leak.

In 1944 Charles Child (New York City, New York) reported a series that included six PDs [20]. He described an end-to-end invaginating pancreaticojejunostomy, which was performed in the latter four cases, with only one pancreatic fistula. Child also advocated for reconstruction which placed the GJ distal to the biliary anastomosis.

As the anatomic definition of a PD became accepted, the evolution of pylorus-preserving PD warrants mention. Although multiple early surgeons attempted to preserve the duodenum, Whipple had advocated for a distal gastrectomy in his latter publications. It is likely that this practice stemmed from his initial one-stage PD in which he had already transected the stomach. The first modern, anatomic pylorus-preserving PD was performed in 1944 by Kenneth Watson (Surrey, United Kingdom) for ampullary cancer [21]. The operation was performed in two stages as the patient had long-standing jaundice. First, a cholecystojejunostomy was performed using a loop, followed a month later by resection. The duodenum was divided 1 inch distal to the pylorus, with reconstruction of a Roux limb to the hepaticojejunostomy (HJ) and duodenojejunostomy (DJ) and closure of the pancreatic stump. Watson intentionally avoided partial gastrectomy in order to "ensure maximal gastric digestion of protein and carbohydrate" and to "prevent the formation of an anastomotic ulcer." However, the patient had difficulty with enteral intake and required jejunostomy tube placement, as well as operative drainage of an abscess, and was hospitalized over 3 months.

Over three decades later in 1978, William Traverso and William Longmire renewed interest in pylorus-preserving pancreatoduodenectomy (PPPD) [22], especially when performing the operation for benign disease. They cited a goal to decrease the rate of marginal ulceration and improve nutrition and reported two cases of pylorus preservation with transection 4 cm distal to the pylorus. This variation was first attempted in 1977 but intraoperatively converted to a classic PD due to ischemia. Their first successful PPPD underwent the operation for an obstructing pseudocyst in the setting of acute or chronic alcoholic pancreatitis and the second patient for a duodenal cancer. Both patients gained weight after discharge, and neither reported steatorrhea although both took pancreatic enzymes. In their follow-up of 18 patients who underwent PPPD, no marginal ulcer or postgastrectomy syndrome was noted, and the operation is widely used today [23].

It is worth emphasizing that the success and acceptance of radical resections of the pancreatic head and periampullary pathology owe a great debt to the advancements in medicine and technologic advancements in other fields. The ability to provide blood transfusions for intraoperative and postoperative resuscitation made the operation remarkably safer and overcame earlier mortalities related to hemorrhage [10, 17].

The isolation and availability of vitamin K resulted from work performed by Henrik Dam and led to the recognition that it was a crucial factor for coagulation. It became widely available in 1939 [11], and this discovery would lead to a share of the Nobel Prize in Physiology or Medicine in 1943 [24]. Whipple attributed the discovery and use of vitamin K starting in 1940 to normalize coagulation profile in jaundiced patients and attributes this discovery to the ability to transition from a two-stage to one-stage operation [10].

The isolation of both insulin and pancreatic enzyme replacement in the early 1900s enabled the management of postoperative endocrine and

exocrine insufficiency associated with pancreatic resections and ligation of the pancreatic duct. For example, Tenani administered raw animal pancreas for his initial PD [11], and Whipple advocated for the use of "pancreatic extracts" as he did in those "who show fat indigestion" [14].

Improvements in surgical practice evolved with radiographic and endoscopic advancements as well. Historically, the diagnosis of periampullary cancer relied on physical exam and upper gastrointestinal studies using fluoroscopy or contrast studies. Imaging was unreliable to diagnose periampullary cancers and gave little information regarding metastases which would preclude resection [2].

Computed tomography (CT) was first performed clinically in 1971 (London, England) [25] and would become critical to the diagnosis and management of pancreatic malignancies and resections. Over the next several decades, as resolution improved, and scan time decreased, the diagnosis of periampullary diseases improved, and more critically, the ability to diagnose and treat postoperative complications without needing to reoperate enabled improving outcomes [4]. Modern pancreatic surgery relies on radiologic assistance for drainage of collections and angioembolization for hemorrhage, all of which has decreased the need for operative intervention [26].

Over the next decades, technologic advancements took a back seat to system shifts which resulted in lower mortality and morbidity. With more surgeons performing PDs, gradual improvements in outcomes were seen. Kenneth Warren at the Lahey Clinic reported 218 PDs between 1942 and 1961 with an 11.9% postoperative mortality that fell to 10.9% when total pancreatectomies were excluded [16]. High-volume centers and surgeons saw monumental improvements in outcomes with a 30-day mortality of 1.4% by surgeons such as John Cameron [FIG] at high-volume centers [27]. The benefit of centralization of expertise has been consistently demonstrated around the world [11].

As expertise and experience accumulated, the question of vascular resections took hold. The first was reported by George Moore in 1951 (Minneapolis, Minnesota) with a resection of a 3 cm segment of the SMV and primary end-to-end anastomosis which was described by the authors as "supplementary and futile" [11, 28]. Reconstruction proceeded with a choledochojejunostomy, PJ, and GJ. The patient initially recovered well and was discharged on postoperative day 10 but returned over a month later with fevers and dehydration. Autopsy demonstrated carcinomatosis and large pulmonary emboli, although all anastomoses and the vein repair were intact. The authors questioned whether aggressive surgical therapy was warranted in a cancer whose biology often implied grossly undetectable metastatic disease.

Subsequently, Joseph Fortner reported in 1976 (New York City, New York) a series of 18 patients from Memorial Sloan Kettering Cancer Center who underwent "regional pancreatectomy" which included total or subtotal pancreatectomy with vein resection and retroperitoneal lymphadenectomy [[11, 29]. The 30-day mortality was 16.6% with a 62% 1-year actuarial survival. The MD Anderson group compared isolated venous resection and found no difference in perioperative outcomes or long-term survival compared to patients who underwent PD without vein resection [30].

2.3 Current Controversies

The Achilles' heel of modern pancreatic surgery remains the pancreatic anastomosis and the high rate of postoperative pancreatic fistula (POPF), which is defined by the International Study Group on Pancreatic Fistula (ISGPF) as any drain output on POD 3 with drain amylase 3 greater than the serum activity [31]. Risk factors for POPF include soft pancreatic texture, small duct size, pathology, surgeon experience, type of anastomosis, blood loss, advanced age, and coronary artery disease [26, 32]. Pancreatic fistulae often beget additional complications and a prolonged recovery. A wealth of work has been performed examining the various techniques in the pancreatic-enteric anastomosis, starting with no anastomosis in the original Whipple description to various modern variations of technique,

which will be addressed in later chapters, including pancreaticojejunostomy versus pancreaticogastrostomy, duct-to-mucosa versus invaginating anastomosis, use of sealants, internal stenting versus external drainage, minimally invasive versus open, and use of somatostatin analogues.

Pancreaticogastrostomy was first reported in 1946 by John Waugh and O. Theron Clagett of the Mayo Clinic (Rochester, Minnesota) in a summary of 30 cases performed to date at their institution [33]. Their early experience, like Whipple's, involved closure of the pancreatic stump in 17 patients. Twelve patients in the latter part of the series underwent pancreaticojejunostomy, and 1 case of the 30 involved a pancreaticogastrostomy although no clear explanation was given for this deviation.

A number of randomized trials have been performed to compare PJ versus PG, and a recent meta-analysis included 7 trials with a total of 1121 patients [34]. PG was associated with fewer POPFs, grade B and C POPFs (clinically relevant POPFs, CR-POPF), and hospital length of stay, but there was no difference in overall morbidity, reoperation, or mortality. Individual series examining PG versus modified Blumgart PJ noted a significant decrease in CR-POPF for intermediate- (6 vs. 21%) and high-risk (14 vs. 47%) patients [35, 36] based on the Fistula Risk Score [32].

For surgeons who routinely perform a PJ, the technique has undergone several iterations although none has been demonstrated to be unequivocally superior. The two most common techniques are duct-to-mucosa and invagination, but the data are mixed as to the superiority of either technique [37]. A meta-analysis of randomized controlled trials (RCTs) included 5 trials with 654 patients [38] and showed no difference in POPF, delayed gastric emptying (DGE), morbidity, length of stay (LOS), or mortality comparing the two techniques. Invagination did appear to be associated with fewer CR-POPFs in two studies in which the ISGPF definition was applied.

Another topic of debate has been the role of stenting of the pancreatic duct. Internal stenting was addressed in a randomized controlled trial of 238 patients [39]. There was no statistically significant difference in POPF for the internally stented versus non-stented patients and no differences in the outcome for those who did develop a POPF. A meta-analysis of RCTs comparing external stent to no stent showed decreased POPF (RR = 0.57, 95% CI = 0.41–0.80) and decreased morbidity and length of stay with external stents [40].

A systematic review of RCTs included 1018 patients from 8 studies [41]. Meta-analysis found no difference in POPF, morbidity, or mortality but found a decreased length of hospital stay by 4 days with stenting. No difference was found when comparing internal versus external stents with regard to development of POPF or other morbidities in this review.

Recently, interest has been renewed in examining the placement of operative drains and postoperative management of drains to reduce morbidity. Several trials have demonstrated increased mortality in patients without drains despite fewer morbidities and no difference in POPF rate [37]. A protocol with omission of drains in low-risk patients based on the Fistula Risk Score and early removal of drains on POD 3 in patients with POD 1 drain amylase < 5000 U/L demonstrated lower CR-POPF rates, complications, and length of stay [42]. There is currently no consensus on the usage of drains, the number, or the optimal time for removal.

Another adjunctive therapy that has been used to reduce POPF is perioperative somatostatin usage. Eleven RCTs have been reported with mixed results and continued debate [26]. There appears to be a decrease in POPF rate with no effect on CR-POPF rate [37]. A 2013 Cochrane review of 21 trials for evaluation of prophylactic use of a somatostatin analogue included 2,348 patients and found lower morbidity in the somatostatin analogue group (RR0.70, 95% CI 0.61–0.80) but no difference in reoperation, length of stay, or mortality [43].

Intraoperatively, fibrin sealants have been explored in a limited extent for proximal and distal pancreatic resection without substantial success [44]. Likewise, the use of the round ligament of the liver as a vascular pedicle to cover the PJ has been reported without improvement in

outcomes [37, 45]. Duct occlusion likewise has not been shown to decrease morbidity or mortality but impairs exocrine function [37].

Beyond simply the technical details of pancreatic resections and perioperative management, there is consistent evidence that high-volume centers and surgeons in this demanding specialty can affect morbidity, mortality, and outcomes. Surgeon and hospital volume are widely accepted as a reliable predictor of outcomes. In a pooled analysis of 58,023 PDs, hospital volume was inversely associated with mortality in a stepwise fashion [46].

2.4 Minimally Invasive Pancreatectomy

The first laparoscopic PD was performed in 1992 by Michel Gagner and Alfons Pomp (Montreal, Canada) [47]. The patient had chronic pancreatitis involving the pancreatic head and also pancreatic divisum, with failure of previous transduodenal sphincteroplasty. The operation was performed in 10 h and completed entirely intracorporeally, with the specimen extracted via a 3 cm epigastric incision. Postoperative course was complicated by delayed gastric emptying requiring prolonged nasogastric decompression and parenteral nutrition, and jejunal ulceration was managed medically.

Robotic platforms have also proliferated in the past two decades with increasing surgeon experience in the technology. Proponents cite improved visualization with depth perception and magnification, stabilization, and improved ergonomics [48]. The first robotic PD series was reported by Cristoforo Giulianotti in 2003 (Grosseto, Italy) [49] and included eight patients. The initial experience utilized laparoscopic mobilization with robotic reconstruction, and the final two cases used full robotic mobilization and reconstruction. The pancreatic stump was closed in all cases by injection of surgical glue into the duct and suture closure, and three POPF were observed. One case was converted to an open laparotomy due to portal vein involvement, and there was a single postoperative mortality. Robotic PD compared to open was associated with longer operative time (490 vs. 250 min) but similar length of stay (20 vs. 18 days) in this series.

A recent single institution series of 250 robotic pancreatic resections including 132 PDs demonstrated a 30-day mortality of 1.5%, major morbidity of 21% (Clavien-Dindo grade III or IV complications) with a marked improvement after 100 cases, and similar profile of pancreatectomy-specific complications compared to modern open PD series [50].

A systematic review of laparoscopic, robotic, and hand-assisted PDs of a series of at least 10 cases included 32 studies for analysis, encompassing 2209 patients [35, 36]. The weighted average operative time was 427 minutes, estimated blood loss was 289 mL, and the conversion rate was 17.8%. The rate of Clavien-Dindo grade III and higher complications was 14.3%, the rate of CR-POPF was 8.0%, and postoperative mortality was 2.3%. A series that included comparison to an open group demonstrated a longer operative time for minimally invasive PD but less blood loss and length of hospital stay. Long-term outcomes regarding recurrence and survival are accumulating and will be forthcoming to evaluate the MIS approach.

2.5 Other Pancreatic Resections

The majority of our discussion focuses on the evolution of PDs, but it is worthwhile to discuss total pancreatectomy in brief. The first successful total pancreatectomy was reported in 1943 by Eugene Rockey (Portland, OR) for a pancreatic body cancer [51]. The patient initially underwent cholecystoduodenostomy and the definitive resection delayed due to lack of blood availability for transfusion. Three days later, the patient underwent total pancreatectomy with distal gastrectomy and duodenectomy and reconstruction using a GJ and choledochojejunostomy distal to the GJ. The initial postoperative course was marred by hypoglycemia due to excessive insulin administration. The patient expired on postoperative day 15 with autopsy showing peritonitis with bilious ascites. The cause of death was thought to

be leakage from the distal CBD stump and resultant peritonitis.

The first long-term survivor of a total pancreatectomy was reported by James Priestley in 1944 (Rochester, MN) [52]. Priestley performed a total pancreatectomy for a symptomatic insulinoma. At the time of exploration, no mass was palpable in the pancreas, and the surgeon elected to perform a total pancreatectomy. A distal antrectomy was performed with resection of the first and second portions of the duodenum. A retrocolic GJ was performed, as well as a cholecystogastrostomy, and the distal duodenum was closed. Pathology revealed an 8 mm pancreatic head insulinoma. The patient was alive 16 months after the operation.

Conclusions

The history of pancreatic surgery tells a story of ingenuity born of necessity and a mentality to continually push the boundaries of what was considered possible or advisable. The Whipple operation has been changed and reshaped by many. Even the current practice in pancreatic surgery varies widely by region [53], as evidenced by a recent survey of 891 surgeons around the world. Pancreaticojejunostomy is favored by 88.7% with the majority employing a two-layered duct-to-mucosa technique, stents are utilized by 73.6% either selectively or in all cases with the majority favoring internal stents, biologic sealants are used by 34.9%, and autologous tissue reinforcement is used by 38.3%. Drains are used routinely by 59.2% and selectively by 26.9%, with one-third placing one drain and two-thirds placing two drains.

As before, the success of pancreatic surgery relies on careful diagnosis, meticulous technique, and astute postoperative management. The future of pancreatic surgery will be challenged by an emphasis on multimodal care for biologically aggressive tumors, surveillance and resection of an increasing number of premalignant pancreatic lesions, and expansion of new technologies. The technical principles have been undergoing evolution since the time of Allen Whipple, now combined with therapies tailored to patient risks and biology, and advances in chemotherapy will enable surgeons to bring about continued improvement in patient outcomes.

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3 Japanese Classification and Staging for Pancreatic and Periampullary Cancers

Satoshi Hirano and Takahiro Tsuchikawa

3.1 General Principles of the Japanese Classification

The categories of cancers are recorded in terms of the upper-case letters T, N, and M, in accordance with the International Union Against Cancer (UICC) and American Joint Committee on Cancer (AJCC) systems [1, 2] for pancreatic and biliary tract cancers.

Stages of disease are determined based on the assessments of three components: T, the contiguous extent of the primary tumour; N, the absence or presence of regional lymph node involvement; and M, the absence or presence of distant metastasis, including in those lymph nodes that are situated beyond regional lymph nodes. The extent of disease is expressed by the addition of Arabic numerals following the letter (e.g. T1, M0); wherever information on a specific category is unknown, "X" is used.

The clinical classification is labelled by the addition of the lower-case letter "c" as a prefix, whereas the pathological classification is denoted by the prefix "p". The clinical classification is based on the information acquired before the initiation of primary treatment, and the pathological classification is based on evidence acquired from the pathological examination of resected specimens. The classification for pancreatic cancers has newly defined the addition of the prefixes "s" and "f" for denoting the surgical and final findings, respectively. Surgical classification is based on intraoperative findings, including results from frozen sections or cytology diagnoses; final classification is based on the comprehensive judgement of clinical, surgical, and pathological findings (Table 3.1).

When classification is performed during or following chemotherapy, including in the neoadjuvant setting, "y" is added as a prefix to indicate yielding to treatment (e.g. ycT, ypN). Recurrent tumours, when classified after disease-free intervals, are identified by the prefix "r". The clinical classification of a recurrent tumour is described using the letters "rc" as prefix, and "rp" is used to indicate the pathological classification of recurrent tumours that have been surgically resected. The prefix "a" indicates that classification was first determined at autopsy. If there is any uncertainty among the T, N, or M categories, the less advanced category should be assigned.

3.2 Japanese Classification and Staging of Pancreatic Cancers

In 2016, the Japanese Pancreas Society (JPS) published a new version of the Japanese classification of the General Rules for the Study of

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Table 3.1 Data sources of each type of classification (reprint from [3], revised)

	Clinical classification	Surgical classification	Pathological classification	Final classification
Data source	Physical findings	Surgical findings	Histological examination of surgically or endoscopically resected specimen	Comprehensive judgement of clinical, surgical, and pathological findings
	Imaging/endoscopic (laparoscopic) findings	Intraoperative image findings		
	Biopsy/cytology of primary site	Intraoperative biopsy/cytology findings		
	Biochemical/ biological examination			
	Others (e.g. genetic examination)			

Pancreatic Cancer (the 7th edition) [3]. An English version of this 7th edition is described here.

3.2.1 Definition of the Anatomy of the Pancreas

The pancreas is anatomically divided into three regions, namely, the pancreas head (Ph), pancreas body (Pb), and pancreas tail (Pt). The lines dividing the Ph and Pb and the Pb and Pt are the left borders of the portal vein and aorta, respectively (Fig. 3.1).

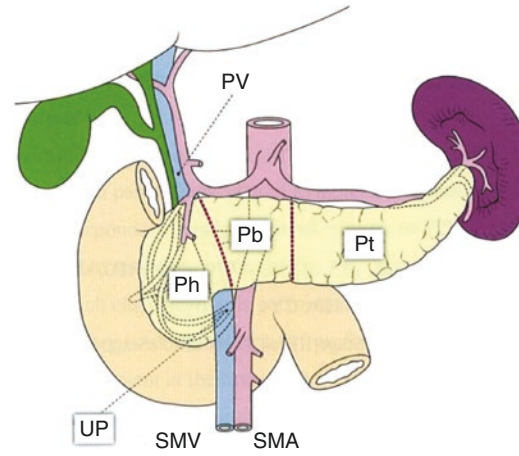

Fig. 3.1 Parts of the pancreas (reprint from [3]). The pancreas is anatomically divided into three regions, namely, the pancreas head (Ph), pancreas body (Pb), and pancreas tail (Pt)

3.2.2 Description of Primary Tumours of the Pancreas

3.2.2.1 Tumour Location

If more than one anatomical region is involved in the tumour, all regions should be recorded in the order of involvement, beginning with the region in which the bulk of the tumour is located (e.g. Phb, Pbht).

3.2.2.2 Size and Number of Lesions

The greatest dimension of each lesion should be recorded as tumour size (TSx [y mm]), per the definition shown below. For patients with multiple tumours, the number of tumours and the size of each lesion should be recorded.

TS1: Less than 20 mm (TS1 ≤ 20 mm)
TS2: Between 20 and 40 mm (20 mm < TS2 ≤ 40 mm)
TS3: Between 40 and 60 mm (40 mm < TS2≤ 60 mm)
TS4: Over 60 mm (TS4 > 60 mm)

In cases of mucinous cystadenocarcinomas, the maximum diameters of these tumours should

be recorded. In cases of intraductal papillary mucinous carcinomas, the TS including the intraductal spread in the main duct type of carcinomas and the size of the dilated branch duct in the branch type should be recorded. The invasive area should be added separately to the description of TS (e.g. TS2 (35 mm), i-TS (15 mm)).

3.2.2.3 Macroscopic Types

Macroscopic types of primary tumours are classified per their morphologies into masked, nodular, infiltrative, cystic, ductectatic, mixed, and unclassifiable (Table 3.2).

3.2.2.4 Contiguous Extent of the Primary Tumour (T-Category)

As demonstrated below, the contiguous extents of the primary tumours are recorded as the T-category. The factors demonstrating the local extent of the tumours are recorded with the T-category, namely, CH, DU, S, RP, PV, A, PL, and OO.

TX: Primary tumour cannot be assessed
T0: No evidence of primary tumour
Tis: Carcinoma in situ (corresponding to non-invasive mucinous cystic neoplasms, intraductal papillary mucinous neoplasms, or high-grade PanIN lesions)
T1: Tumours that are localized to the pancreas and are 20 mm or less in size
T1a: Tumours 5 mm or less in maximum size
T1b: Tumours more than 5 and 10 mm or less in maximum size
T1c: Tumours more than 10 and 20 mm or less in maximum size
T2: Tumours localized to the pancreas and more than 20 mm in size
T3: Tumours extending beyond the pancreas (at least one of the following factors is positive: CH, DU, S, RP, PV, A, PL, OO) without invasion into the celiac or the superior mesenteric arteries
T4: Tumours invading into the celiac artery, the superior mesenteric artery, or a combination of both

Table 3.2 Macroscopic types of the pancreatic cancer (reprint from [3], revised)

Masked type	Macroscopically unidentifiable tumours
Nodular type	Tumours with clear margin
Infiltrative type	Tumours with unclear margin, invaded diffusely into surrounding tissue
Cystic type	Tumours composed by cystic structure (e.g. cystadenocarcinoma) excepting secondary cysts due to tumour necrosis, retention cysts, and pseudocysts
Ductectatic type	Tumours mainly composed with dilatation of the duct usually due to hypersecretion of mucin
Mixed type	Tumours composed with more than two macroscopic types
Unclassifiable type	Tumours that cannot be classified into any of the above types

3.2.2.5 Factors of the Local Extent of the Tumour

Each factor is followed by "0", "1", or "X", which denotes positive, negative, or undeterminable, respectively (e.g. CH0, DU1, SX, etc.).

CH: Infiltration into the bile duct (into the fibromuscular layer or deeper, as seen during histopathological investigation)
DU: Infiltration into the duodenum (into the muscular layer or deeper, as seen during histopathological investigation)
S: Infiltration into the fibrous connective tissue or the fat tissue in the ventral side of the pancreas, including the exposure of the tumour on the serous membrane of the pancreas
RP: Infiltration into the fibrous connective tissue or the fat tissue in the dorsal side of the pancreas
PV: Infiltration into the portal system (into the adventitia or deeper, as seen during histopathological investigation)
A: Infiltration into the superior mesenteric (Asm), celiac (Ace), common hepatic (Ach), or the splenic (Asp) arteries (into the adventitia or deeper, as seen during histopathological investigation)
PL: Infiltration into the extrapancreatic nerve plexus (Fig. 3.2), which is divided into seven anatomical regions: the plexus around the celiac artery (PLce), the plexus around the

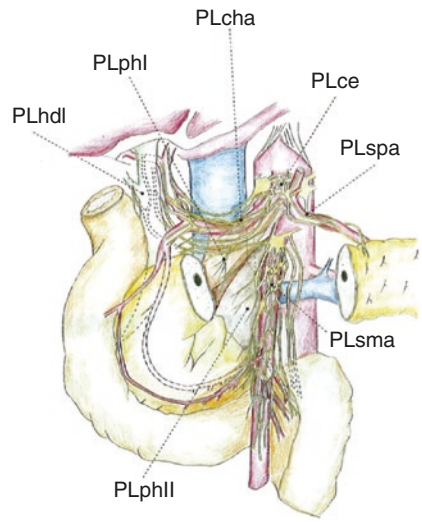

Fig. 3.2 Extrapancreatic nerve plexuses (reprint from [3]). The extrapancreatic nerve plexuses are divided into seven anatomical regions, namely, PLce (celiac artery), PLsma (superior mesenteric artery), PLcha (common hepatic artery), PLspa (splenic artery), PLhdl (hepatoduodenal ligament), PLph1 (first pancreatic head plexus), and PLph2 (second pancreatic head plexus)

superior mesenteric artery (PLsma), the plexus around the common hepatic artery (PLcha), the plexus around the splenic artery (PLspa), the plexus in the hepatoduodenal ligament (PLhdl), the first portion of the pancreatic head plexus (PLph1) located between the PLce and the dorsal side of the pancreatic head, and the second portion of the pancreatic head plexus (PLph2) located between the PLsma and the uncinate process

3.2.2.6 Description of Lymph Node Metastasis (N-Category)

In the Japanese classifications of cancers, lymph nodes are given station numbers per their anatomical locations as shown in Table 3.3 and Fig. 3.3. The detailed definitions of lymph nodes 12, 14, and 16 are schematically demonstrated in Figs. 3.4 and 3.5. The regional lymph nodes of the pancreas include the nodes surrounding the entire pancreas and are defined as lymph nodes 5, 6, 7, 8a, 8p, 9, 10, 11p, 11d, 12a, 12b, 12p, 13a, 13b, 14p, 14d, 17a, 17b, and 18. Cancers that have spread to lymph nodes other than the regional lymph nodes are considered distant metastases (M1) (see Sect. 3.2.4).

Per this new version of the classification, the definition of regional nodes corresponding to the location of the tumour was rescinded. Instead, the total number of metastatic lymph nodes has been considered for defining the severity of lymph node metastasis (e.g. N1a, N1b), and this reflects the staging of the disease.

NX: Regional lymph node cannot be assessed
N0: No regional lymph node metastasis
N1: Regional lymph node metastasis
- N1a: 1–3 lymph node metastases in the regional lymph nodes
- N1b: More than four lymph node metastases in the regional lymph nodes

Table 3.3 Anatomical definition of lymph node stations (reprint from [3])

No.	Definition
1	Right paracradial LNs
2	Left paracradial LNs
3	LNs along the lesser curvature of the stomach
4	LNs along the greater curvature of the stomach
5	Suprapyloric LNs
6	Infrapyloric LNs
7	LNs along the trunk of the left gastric artery
8	LNs along the common hepatic artery
8a	LNs on the anterosuperior surface
8p	LNs on the posterior surface
9	LNs around the celiac artery
10	LNs at the splenic hilum
11	LNs along the splenic artery
11p	LNs on the proximal part
11d	LNs on the distal part
12	LNs in the hepatoduodenal ligament
12a	LNs along the proper hepatic artery
12p	LNs along the portal vein
12b	LNs along the bile duct
13	LNs on the posterior surface of the head of the pancreas
13a	LNs on the cranio-posterior surface of the head of the pancreas
13b	LNs on the caudal-posterior surface of the head of the pancreas
14	LNs at the root of the superior mesenteric artery

(continued)

Table 3.3 (continued)

No.	Definition
14p	Proximal LNs from the origin of the superior mesenteric artery to the origin a of the inferior pancreaticoduodenal artery
14d	Distal LNs from the origin a of the inferior pancreaticoduodenal artery to the origin of the middle colic artery
15	LNs along the middle colic artery
16	LNs along the abdominal aorta
16a1	LNs in the diaphragmatic aortic hiatus including infradiaphragmatic LNs predominantly along the subphrenic artery
16a2	LNs along between the upper border of the origin of the celiac artery and the lower border of the origin of the left renal vein
16b1	LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery
16b2	LNs between upper border of the origin of the inferior mesenteric artery and the aortic bifurcation
17	LNs on the anterior surface of the head of the pancreas
17a	LNs on the cranio-anterior surface of the head of the pancreas
17b	LNs on the caudal-anterior surface of the head of the pancreas
18	LNs along the inferior border of the pancreatic body and tail excluding LNs at the root of the superior mesenteric artery (#14)

3.2.2.7 Description of Distant Metastasis (M-Category)

Metastases to distant organs and to lymph nodes other than regional lymph nodes are considered distant metastases.

M0: No distant metastasis
M1: Distant metastasis

The category M1 may be further classified by the following notations: PUL (pulmonary), MAR (bone marrow), OSS (osseous), PLE (pleura), HEP (hepatic), PER (peritoneum), BRA (brain), ADR (adrenals), LYM (lymph nodes), SKI (skin), and OTH (others). In distant metastases, peritoneal and hepatic metastases are especially documented as mentioned below:

P0: No peritoneal metastasis
P1: Peritoneal metastasis
H0: No hepatic metastasis
H1: Hepatic metastasis

The performance and the results of peritoneal cytology are described as indicated below. The positive results of these should not be treated as distant metastases.

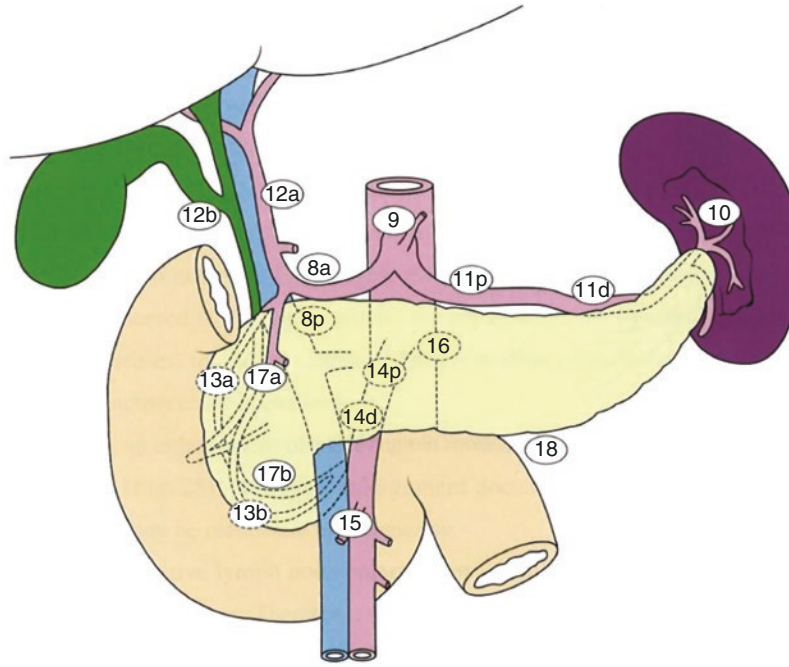

Fig. 3.3 Lymph node station numbers in relation to the pancreas (reprint from [3])

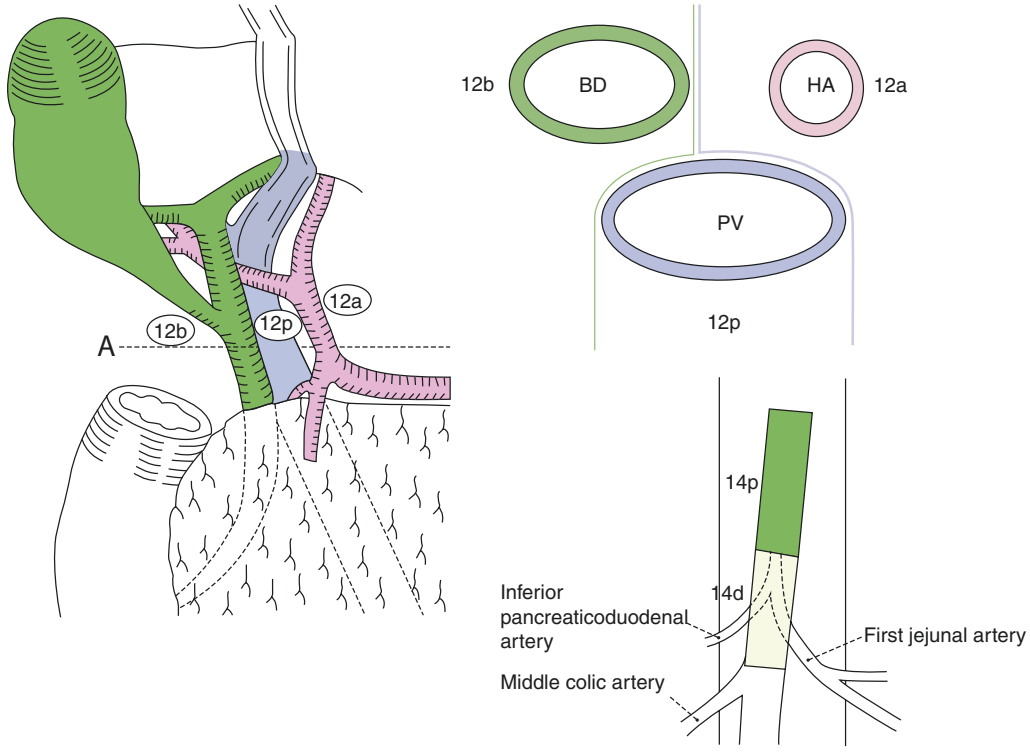

Fig. 3.4 The locations and boundaries of lymph node stations within the hepatoduodenal ligament and along the superior mesenteric artery (reprint from [3]). The definitions of the lymph nodes 12a, 12b, and 12p are determined by their positions related to the blood vessels and the bile duct. The boundary between the lymph nodes 14p and 14d is the midpoint of the distance between the root of the superior mesenteric artery and the origin of the middle colic artery

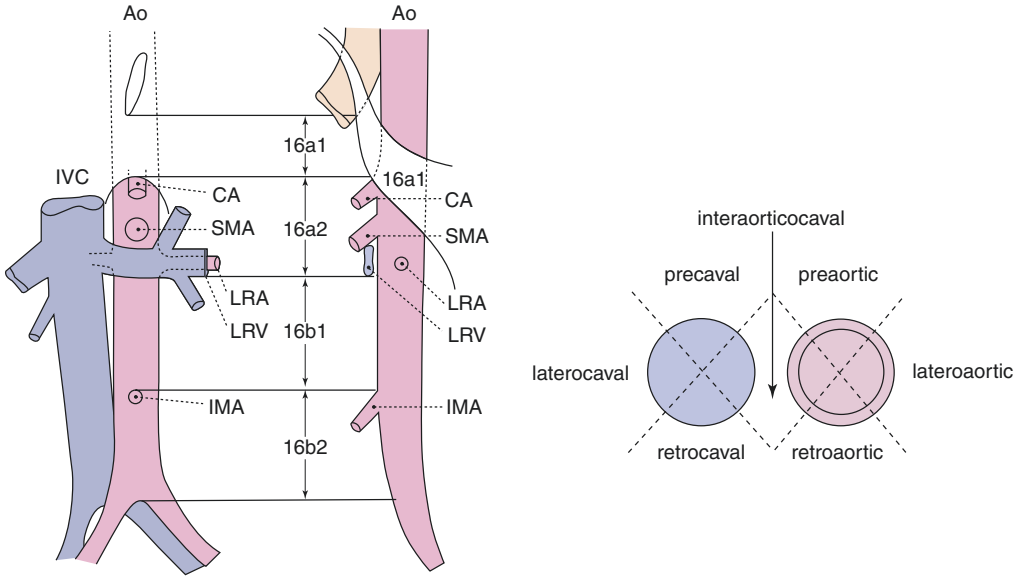

Fig. 3.5 The location and boundaries of lymph node stations around the abdominal aorta (reprint from [3]). The detailed definitions of lymph nodes 16a1, 16a2, 16b1, and 16b2 are determined by their positions related to the branches of the abdominal aorta and the left renal vein. Each node should be accompanied by directional information such as "pre-", "latero-", or "retro-" or prefixing with "caval", "aortic", or "interaorticocaval"

CYX: Peritoneal cytology not performed
CY0: Negative for peritoneal cytology
CY1: Positive for peritoneal cytology

3.2.2.8 Stage Grouping of the Pancreatic Cancers (Table 3.4)

The new Japanese classification comprises a stage grouping that references the classification of the resectability of tumours, which can indicate therapeutic strategies rather than the prognoses of patients. The lesions diagnosed as Stage 0, I, or II are defined as "Resectable", Stage III as "Borderline resectable", and Stage IV as "Unresectable". Resectability was defined accordingly, as described in the following section.

3.2.2.9 Resectability Classification

Resectability was originally established for the new classification and is classified into three categories based on findings from the contrast enhanced, multiphasic, thin-section computed tomography images: resectable (R), borderline resectable (BR), and unresectable (UR).

Resectable (R)

1. Tumours without contact with the superior mesenteric (SMV) or the portal (PV) veins
2. Tumours in contact with SMV or PV in less than 180° without occlusion
3. Tumours invading the superior mesenteric (SMA), the celiac (CA), or the common hepatic (CHA) arteries

Borderline Resectable (BR)

BR lesions are stratified into two categories, namely, BR-PV and BR-A as described below. If the tumour has both factors, BR-PV and BR-A, the lesion is treated as BR-A.

BR-PV: Tumours in contact with SMV or PV in 180° or more without contact with SMA, CA, or CHA. This involvement does not exceed the inferior border of the third portion of the duodenum.

BR-A

1. Tumours contact or invade the SMA, the CA, or both in less than 180° without stenosis or deformity of the arteries.
2. Tumours contact or invade the CHA without contact nor invasion of the proper hepatic artery (PHA), the CA, or both.

Unresectable (UR)

UR lesions are stratified into two categories, namely, UR-LA and UR-M, as described below.

UR-LA

1. Tumours contact or invade the SMV or PV in 180° or occlude these vessels. This involvement exceeds the inferior border of the third portion of the duodenum.
2. Tumours contact or invade the SMA, the CA, or both in 180° or more.
3. Tumours contact or invade the CHA with contact or invasion of PHA or CA.
4. Tumours contact or invade the aorta.

UR-M: Tumours with distant metastases, including non-regional lymph node metastases

Table 3.4 Stage grouping of the pancreatic cancer (reprint from [3])

Stage 0	Tis	N0	M0
Stage1A	T1 (T1a, T1b, T1c)	N0	M0
Stage1B	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1 (T1a, T1b, T1c), T2, T3	N1(N1a,N1b)	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

3.2.3 Records of Surgical Procedures for Pancreatic Cancers

3.2.3.1 Surgical Procedures

Pancreatic resection
Palliative resection (bypass surgery, including choledochojejunostomy and gastrojejunostomy)
Exploratory laparotomy and laparoscopy

3.2.3.2 Types of Surgeries for Pancreatic Cancers

PHR: pancreatic head resection
PD: pancreatoduodenectomy
PPPD: pylorus-preserving PD
SSPPD: subtotal stomach-preserving PD
DPPHR: duodenum-preserving PHR
PHRSD: PHR with segmental duodenectomy
DP: distal pancreatectomy
DP (tail/body-tail/subtotal)
SPDP: spleen-preserving DP
DP-CAR: DP with en bloc celiac axis resection
TP: total pancreatectomy
PPTP: pylorus-preserving TP
PSPTP: pylorus-preserving, spleen-preserving TP
DPTP: duodenum-preserving TP
TPSD: TP with segmental duodenectomy

3.2.3.3 Concomitant Resections of Neighbouring Organs

The names of the concomitantly resected organs should be recorded for the duodenum, stomach, colon, spleen, portal venous system, and arteries.

3.2.3.4 Types of Reconstructions Following PD, PPPD, and SSPPD

Types of reconstructions should be recorded per the orders of anastomoses between the jejunum and the pancreas and the bile duct and the duodenum or the stomach from the oral side of the jejunal limb.

Type I (PD1, PPPD-I, SSPPD-I) in the following order: choledochojejunostomy, pancreatojejunostomy, and duodeno- or gastrojejunostomy
Type II (PD-II, PPPD-II, SSPPD-II) in the following order: pancreatojejunostomy, choledochojejunostomy, and duodeno- or gastrojejunostomy
Type III (PD-III, PPPD-III, SSPPD-III)
(a) duodeno- or gastrojejunostomy, pancreatojejunostomy, and choledochojejunostomy (in order)
(b) gastrojejunostomy, choledochojejunostomy, and pancreatojejunostomy (in order)

The types of reconstruction procedures for the residual pancreas are classified as described below. Details of anastomotic procedures include duct-to-mucosa anastomosis, invagination or dunking method, and others.

A: pancreatojejunostomy
B: pancreatogastrostomy
C: pancreatoduodenostomy

3.2.3.5 Grade of Lymph Node Dissection

Lymph node grouping for the pancreas is performed per the type of pancreatectomy (Table 3.5). Grades of lymph node dissections are recorded as follows:

D0: No lymph node dissection
D1: Dissection of Group 1 lymph nodes
D2: Dissection of Group 1 and 2 lymph nodes
D3: Dissection of Group 1, 2, and 3 lymph nodes

3.2.3.6 Evaluation of Residual Tumour

After resecting the tumour, the condition of macroscopic and pathological residue of the tumour is recorded.

RX: Unknown
R0: No residual tumour
R1: Microscopic residual tumour
R2: Macroscopic residual tumour

Table 3.5 Lymph node grouping according to pancreatectomies (reprint from [3])

	Total pancreatectomy	Pancreatoduodenectomy	Distal pancreatectomy
Group 1	#8a, 8p, 10, 11p, 11d, 13a, 13b, 17a, 17b, 18	#8a, 8p, 13a, 13b, 17a, 17b	#10, 11p, 11d, 18
Group 2	#5, 6, 7, 9, 12a, 12b, 12p, 14p, 14d	#5, 6, 12a, 12b, 12p, 14p, 14d	#7, 8a, 8p, 9, 14p, 14d
Group 3	#1, 2, 3, 4, 15, 16a2, 16b1	#1, 2, 3, 4, 7, 9, 10, 11p, 11d, 15, 16a2, 16b1, 18	#5, 6, 12a, 12b, 12p, 13a, 13b, 15, 16a2, 16b1, 17a, 17b

Conditions of the residual tumour in the cut surface of the pancreas and the bile duct and the dissection plane are recorded using the rules described below.

Pancreatic cut end margin: PCM

PCM0: No involvement of pancreatic cut end margin
PCM1: Involvement of pancreatic cut end margin
PCMX: Involvement of pancreatic cut end margin cannot be assessed

Bile duct cut end margin: BCM

BCM0: No involvement of bile duct cut end margin
BCM1: Involvement of bile duct cut end margin
BCMX: Involvement of bile duct cut end margin cannot be assessed

Dissected peripancreatic tissue margin: DPM

DPM0: No involvement of dissected peripancreatic tissue margin
DPM1: Involvement of dissected peripancreatic tissue margin
DPMX: Involvement of dissected peripancreatic tissue margin cannot be assessed

3.2.4 Handling the Resected Specimen of Pancreatic Cancers Obtained by Pancreatectomy

3.2.4.1 Opening of the Duodenum and the Bile Duct (Fig. 3.6)

In principle, the duodenum is opened along the longitudinal direction to observe the papilla of Vater, the accessory papilla, and the mucosa of the duodenum. The common bile duct should be opened from the posterior side.

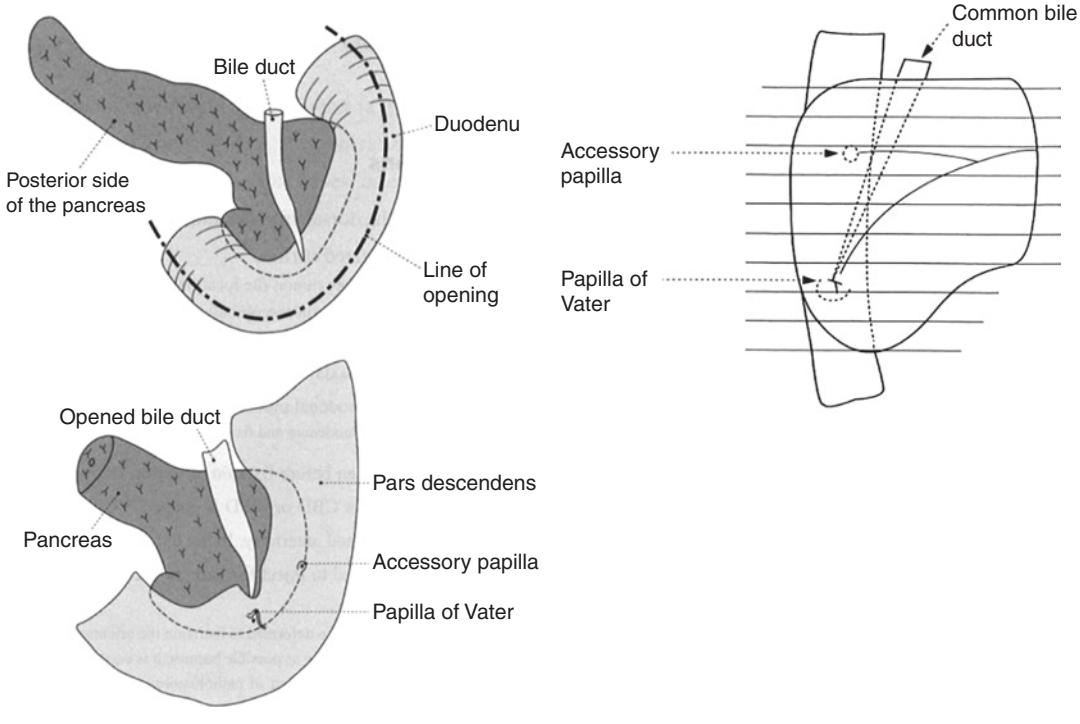

Fig. 3.6 The handling of specimens retrieved by pancreatoduodenectomy (reprint from [3]). (**a**) The duodenum is opened along the longitudinal direction. The common bile duct should also be opened posteriorly. (**b**) The specimen should be sectioned vertically along the longitudinal axis of the duodenum at 5-mm intervals. The centre of the accessory papilla should be divided in each specimen (Fig. 3.6)

3.2.4.2 Sectioning of the Specimen

The specimen obtained by pancreatoduodenectomy should be sectioned vertically along the longitudinal axis of the duodenum, in parallel with the Kerckring's folds, at 5-mm intervals toward the oral and anal sides. The centres of the accessory papilla should be divided in each specimen (Fig. 3.6).

Meanwhile, the specimen obtained by distal pancreatectomy should be sectioned vertically along the longitudinal axis of the pancreas at 5-mm width from the cut end.

3.2.5 Histopathological Classification of Pancreatic Cancers

The histological types of pancreatic tumours are shown in Table 3.6. If an epithelial tumour comprises more than one histological type, the predominant histological pattern should be adopted as representative.

Histological findings are further classified under the following headings: "Cancer Stromal Volume" (see Sect. 3.2.5.1), "Infiltrative Pattern" (see Sect. 3.2.5.2), "Lymph-Vascular and Neural Invasions" (see Sects. 3.2.5.3–3.2.5.5), and "Infiltration into the Main Pancreatic Duct" (see Sect. 3.2.5.3).

Table 3.6 Histologic types of pancreatic tumours and their abbreviations (reprint from [3])

[1] Epithelial neoplasms
A. Exocrine neoplasms
1. Serous neoplasms (SNs)
(a) Serous cystadenoma (SCA)
(b) Serous cystadenocarcinoma (SCC)
2. Mucinous cystic neoplasms (MCNs)
(a) Mucinous cystadenoma (MCA)
(b) Mucinous cystadenocarcinoma (MCC), non-invasive
(c) Mucinous cystadenocarcinoma (MCC), invasive
3. Intraductal neoplasms
(a) Intraductal papillary mucinous neoplasms (IPMNs)
(1) Intraductal papillary mucinous adenoma (IPMA)
(2) Intra ductal papillary mucinous carcinoma (IPMC), non-invasive
(3) Intraductal papillary mucinous carcinoma(IPMC), invasive
(b) Intraductal tubulopapillary neoplasms (ITPNs)
(1) Intra ductal tubulopapillary carcinoma, non-invasive
(2) Intraductal tubulopapillary carcinoma, invasive
(c) Pancreatic intraepithelial neoplasia (PanIN)
(1) Low-grade PanIN
(2) High-grade PanIN
4. Invasive ductal carcinomas (IDCs)
(a) Adenocarcinoma
(i) Well-differentiated type (wel)
(ii) Moderately differentiated type (mod)
(iii) Poorly differentiated adenocarcinoma (por)
(b) Adenosquamous carcinoma (asc)
(c) Mucinous carcinoma (muc)
(d) Anaplastic carcinoma
(i) Anaplastic carcinoma, pleomorphic type
(ii) Anaplastic carcinoma, spindle cell type
(iii) Anaplastic carcinoma with osteoclast-like giant cells
5. Acinar cell neoplasms (ACNs)
(a) Acinar cell cystadenoma (ACA)
(b) Acinar cell carcinoma (ACC)
B. Neuroendocrine neoplasms (NENs)
1. Neuroendocrine tumours (NETs, G1, G2)
2. Neuroendocrine carcinoma (NEC)
C. Combined neoplasms
D. Epithelial neoplasms of uncertain differentiation
1. Solid pseudopapillary neoplasm (SPN)
2. Pancreatoblastoma
E. Unclassifiable
F. Miscellaneous
[2] Non-epithelial neoplasms
Hemangioma, lymphangioma, leiomyosarcoma, malignant lymphoma, paraganglioma, others

3.2.5.1 Cancer Stromal Volume

Medullary type (med): Scanty stroma
Scirrhous type (sci): Abundant stroma
Intermediate type (int): The quantity of stroma is intermediate between the above two types

3.2.5.2 Infiltrative (INF) Patterns of Cancers into the Surrounding Tissues

The most dominant pattern present at the invasive front of the tumour should be judged for classification.

INFa: The tumour shows an expanding growth pattern with a distinct border from the surrounding tissue
INFb: The tumour shows a growth pattern that is intermediate between INFa and INFc
INFc: The tumour shows an infiltrating growth pattern with an indistinct border from the surrounding tissue

3.2.5.3 Lymphatic Invasion

ly0: No lymphatic invasion
ly1: Minimal lymphatic invasion
ly2: Moderate lymphatic invasion
ly3: Marked lymphatic invasion

3.2.5.4 Venous Invasion

v0: No venous invasion
v1: Minimal venous invasion
v2: Moderate venous invasion
v3: Marked venous invasion

3.2.5.5 Intrapancreatic Neural Invasion

ne0: No neural invasion
ne1: Minimal neural invasion
ne2: Moderate neural invasion
ne3: Marked neural invasion

3.2.5.6 Spread of Cancer Within the Main Pancreatic Duct

The distance of the intraductal spread within the main pancreatic duct from the border of the invasive cancer is recorded.

mpd0: No evidence of spread
mpd1: Spread present
mpdx: Spread cannot be assessed

3.2.6 Histologic Classification Based on the Effect of Neoadjuvant Therapies (Table 3.7)

The rate of residual cancer after undergoing preoperative chemotherapies (or radiotherapies) is classified into four grades (Grades 1–4) based on the reaction of tissues upon the destruction of cancer cells. Since the judgement is basically performed only for invasive lesions, the intraepithelial cancer residue after the completion of treatment is classified as Grade 4.

3.2.7 Japanese Classification and Staging for Cancers of the Lower Bile Duct and the Papilla of Vater

In 2015, the 3rd English edition of the Japanese classification of biliary tract cancers [4], which included cancers of the periampullary region (distal bile duct and the papilla of Vater), was released approximately 10 years after the release of the 2nd English edition. It was a near-complete translation of the 6th edition of the General Rules for Clinical and Pathological Studies on Cancer of the Biliary Tract written in Japanese and edited by Japanese Society of Hepato-Biliary-Pancreatic Surgery in 1913 [5].

Table 3.7 Histologic grading for the effect of neoadjuvant therapies (reprint from [3], revised)

	Response	Rate of survivable cancer cells
Grade 1	Poor or no response	≥50%
Grade1a		≥90%
Grade1b		≥50%, <90%
Grade 2	Moderate response	≥10%, <50%
Grade 3	Marked response	<10%
Grade 4	Complete response	No evidence of survivable cancer cell

3.2.8 Definition of the Anatomy of the Distal Bile Duct and the Papilla of Vater

3.2.9 Distal Bile Duct

The distal part of the extrahepatic bile duct (Bd) is anatomically defined by a line that divides the duct equally between the upper margin of the common hepatic duct and the point where the common bile duct enters the wall of the duodenum. This line is principally positioned at the origin of the cystic duct as a guide. The proximal bile duct is named as the perihilar region (Bp) (Fig. 3.7).

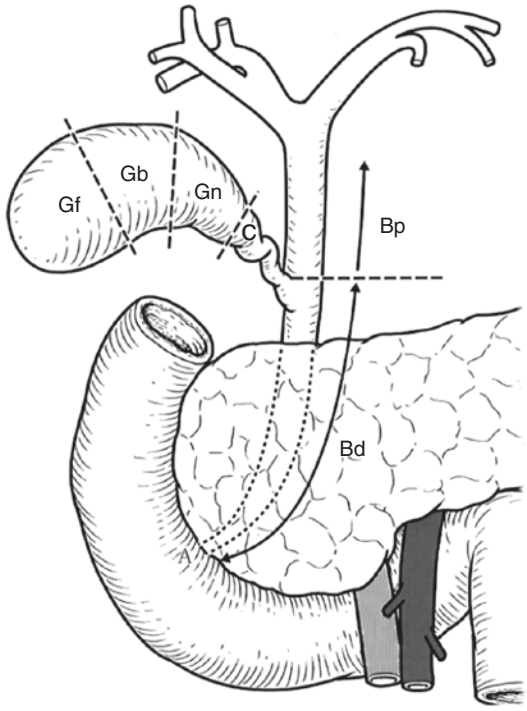

Fig. 3.7 The anatomy of the extrahepatic biliary tracts (reprint from [5], revised). The distal parts of the extrahepatic bile ducts (Bd) are anatomically defined by a line dividing each duct equally between the upper margin of the common hepatic duct and the point where the common bile duct enters the wall of the duodenum. This line is principally positioned at the origin of the cystic duct as a guide. The proximal bile ducts are named as the perihilar region (Bp). *Bd* distal bile duct, *Bh* intrahepatic bile ducts, *Bp* perihilar bile duct, *C* cystic duct, *Gb* body of the gallbladder, *Gf* fundus of the gallbladder, *Gn* neck of the gallbladder

3.2.10 Ampullary Region

The ampullary region (A) is located at the sphincter of Oddi and is composed of a channel leading from the entry point of the common bile duct into the wall of the duodenum to the major duodenal papilla (Fig. 3.8). The ampullary region is composed of four portions: the terminal segment of the common bile duct (Ab), the terminal segment of the main pancreatic duct (Ap), a common channel or an ampulla (Ac), and the major duodenal papilla (Ad). The duodenal surface of the major duodenal papilla is shown as a conical or cylindrical protuberance. A hooding fold of the mucosa that partially covers the superior or cephalad aspect of the papilla and a frenulum-like fold extending from the inferior aspect are not included in the definition of the major duodenal papilla (Fig. 3.8).

3.2.11 Description of Primary Tumour of the Distal Bile Duct

3.2.11.1 Tumour Location

Distal bile duct cancers are defined as tumours arising in the distal bile duct, as shown in Fig 3.7. When it is not possible to determine the exact site of origin, the anatomical region containing the bulk of the tumour may be judged as the primary site.

If more than one anatomical region is involved, all involved regions should be recorded in the order of their involvement, first indicating the region in which the bulk of the tumour is located (e.g. BpdC). Tumour extension into the head of the pancreas or duodenum is recorded as Ph or D. The distinct location of the primary site should be underlined.

In the extrahepatic bile duct, the cross section of the duct wall is divided into four equal parts: the right anterior wall (ra), right posterior wall (rp), left anterior wall (la), and left posterior wall (lp) (Fig. 3.9). All parts that are involved in the tumour should be recorded in the order of involvement, starting with the part in which the bulk of the tumour is located (e.g. rarp). Circumferential involvement is recorded as "circ".

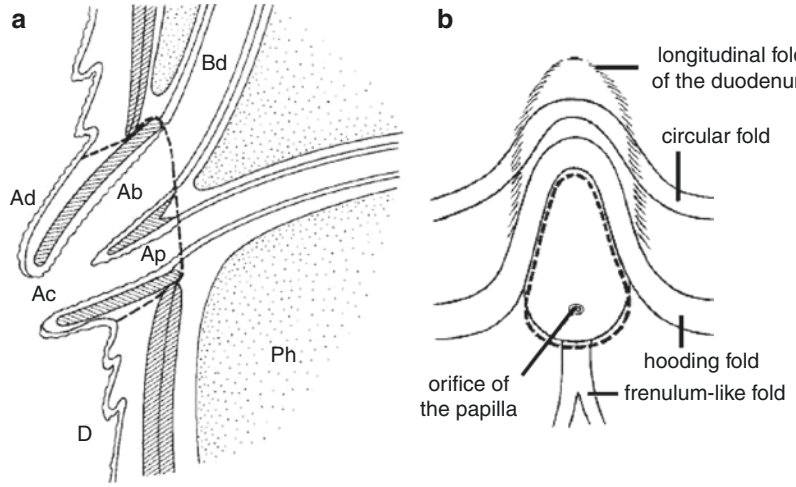

Fig. 3.8 The composition of the ampullary region (reprint from [5]). (**a**) The dotted line indicates the ampullary region that is composed of Ab, Ac, Ad, and Ap. (**b**) The papilla of Vater is covered by the duodenal mucosa (dotted line). *Ab* terminal segment of the common bile duct, *Ac* common channel or ampulla, *Ad* major duodenal papilla, *Ap* terminal segment of the main pancreatic duct, *Bd* distal bile duct, *D* duodenum, *Ph* head of the pancreas

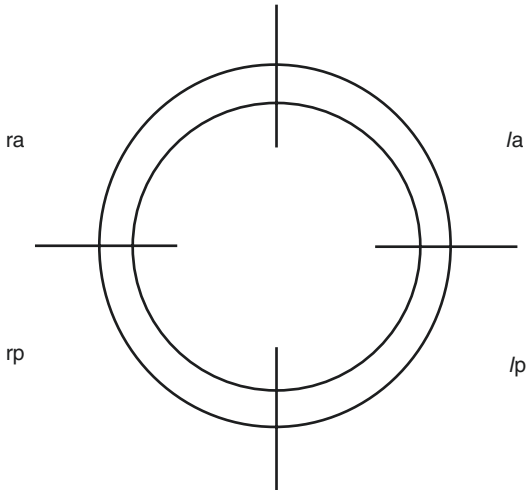

Fig. 3.9 Cross-sectional circumference of the bile duct wall (reprint from [5]). In the extrahepatic bile ducts, the cross-sectional areas of the duct walls are divided into four equal parts: ra, rp, la, and lp. *la* left anterior wall, *lp* left posterior wall, *ra* right anterior wall, *rp* right posterior wall

3.2.11.2 Size and Number of Lesions

For each lesion, the two greatest dimensions should be recorded. In resected specimens, the number of tumours and the two greatest dimensions for each lesion should be recorded after opening the bile duct.

3.2.11.3 Macroscopic Types

Gross tumour morphology is categorized based on either radiological or pathological findings. Macroscopic types of tumours are classified per their morphologies, their heights from the bile duct lumen, and their growth patterns as viewed from the bile duct wall (Table 3.8, Fig. 3.10).

3.2.11.4 Contiguous Extent of the Primary Tumour of the Distal Bile Duct (T-Category)

As described below, the contiguous extent of the primary tumour is recorded as the T-category. Conventional characters denoting the depth of invasion (M, FM, SS, SE [exposed on serosa], SI [invasion to other organs]) may be appended (Fig. 3.11). Lymphatic, venous, or perineural invasions as the invasive fronts are not considered as the depths of invasion.

Tx:	Primary tumour cannot be assessed
T0:	No evidence of primary tumour
Tis:	Carcinoma in situ (carcinomas in situ in the peribiliary glands should be recorded as pTis [M])
T1a:	Tumour confined to the mucosa

Table 3.8 Macroscopic types of the bile duct cancer (reprint from [5], revised)

Papillary type	Papillary or polypoid shape, sharply demarcated from the surrounding mucosa and mainly composed of intramucosal or intraepithelial tumours. This type of tumour contains pedunculated and sessile tumours. The papillary type is subdivided into the papillary-expanding and papillary-infiltrating types according to its growth pattern
Nodular type	Nodular shape, gently continued from the surrounding mucosa and mainly composed of invasive tumours. Nodular tumours with tiny papillary structures on the surface are also included in this category. The nodular type is subdivided into the nodular-expanding and nodular-infiltrating types according to its growth pattern
Flat type	Tumours without elevation. The flat type is subdivided into the flat-expanding and flat-infiltrating types according to its growth pattern, but flat-expanding type is rare. This type implies a traditional infiltrating or diffusely infiltrating type
Others	Tumours that cannot be classified into any of the above types. An ulcerative type or cobblestone appearance can be classified in this category

T1b: Tumour confined to the fibromuscular layer

T2: Tumour invades beyond the bile duct wall into surrounding adipose tissues

T3a: Tumour invades the gallbladder, liver, pancreas, duodenum, or other adjacent organs

T3b: Tumour invades the main portal vein, the inferior mesenteric vein, or the inferior vena cava

T4: Tumour invades the celiac axis, the common hepatic artery, or the superior mesenteric artery

3.2.11.5 Definition of the Bile Duct Wall (Fig. 3.11)

The bile duct wall is composed of the mucosa (M) and the fibromuscular layer (FM) in this T-category. The depth of tumour invasion is denoted as M, FM, SS, SE, and SI.

3.2.11.6 Description of Lymph Node Metastasis (N-Category)

In cases of cancers of the bile duct, the regional lymph nodes are the nodes in the hepatoduodenal ligament (12h, a, b, p, c), the nodes along the common hepatic artery (8a, p), the nodes on the posterior surface of the head of the pancreas

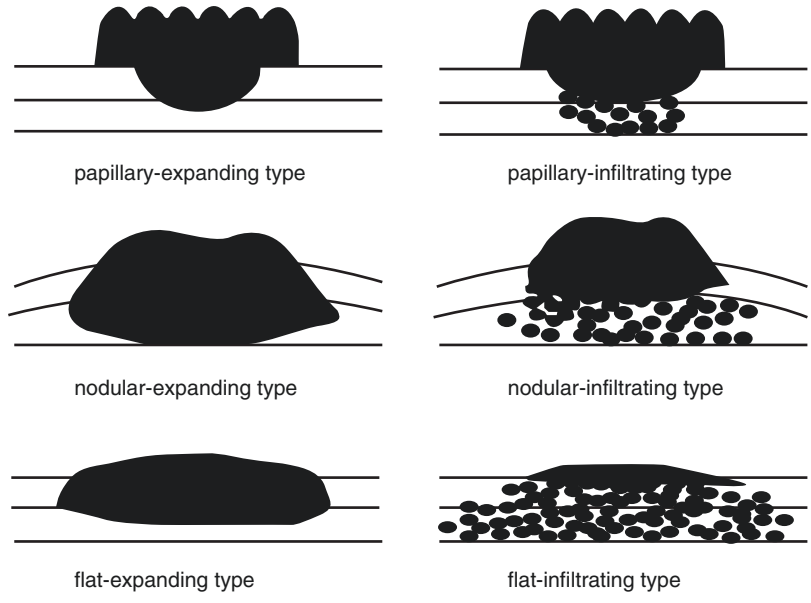

Fig. 3.10 The macroscopic types of the extrahepatic bile duct cancers (reprint from [5]). The macroscopic types of tumours are classified per their morphologies, heights, and growth patterns

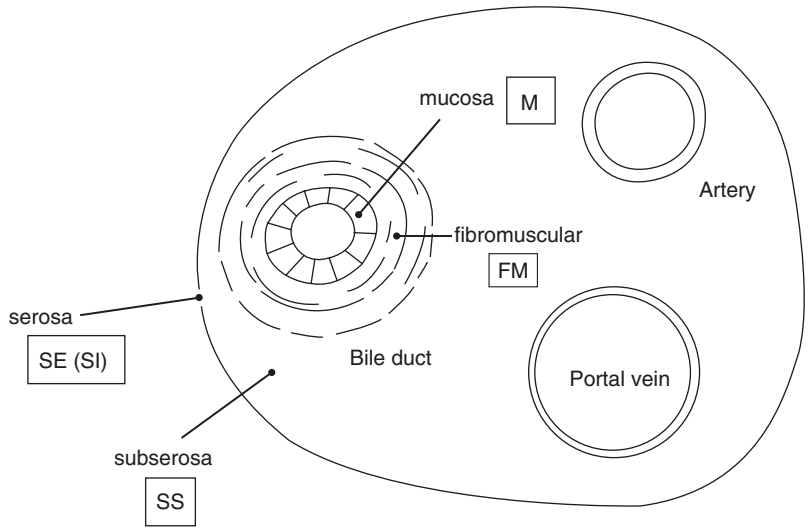

Fig. 3.11 The definition of the bile duct wall (reprint from [5], revised). The bile duct wall is composed of the mucosa (M) and the fibromuscular layer (FM) in this T-category. The depth of tumour invasion is denoted as M, FM, SS, SE, and SI

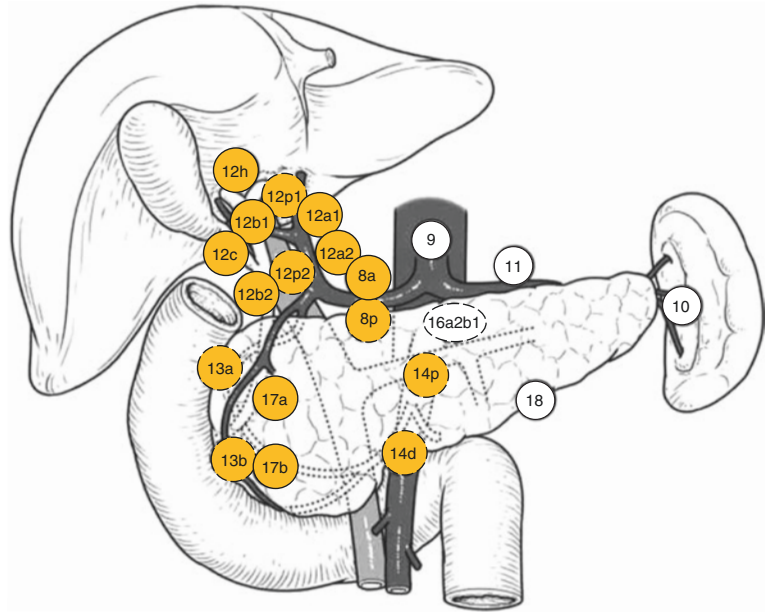

Fig. 3.12 The location and number of lymph node stations related to distal bile duct cancers (reprint from [5], revised). The stations of regional lymph nodes of distal bile duct cancers are coloured in yellow

(13a, b), the nodes on the anterior surface of the head of the pancreas (17a, b), and the nodes at the root of the mesenteric artery (14p, d) (Fig. 3.12). The spread of cancers to lymph nodes other than these regional lymph nodes are considered distant metastases (M1). The number of metastatic nodes and the rate for total number of dissected nodes should be recorded in each station.

Nx: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Regional lymph node metastasis

3.2.11.7 Description of Distant Metastasis (M-Category)

Metastasis to distant organs and to lymph nodes other than the regional lymph nodes are considered distant metastases.

M0: No distant metastasis
M1: With distant metastasis

The category M1 may be further specified by using the following notations: PUL (pulmonary), MAR (bone marrow), OSS (osseous), PLE

(pleura), HEP (hepatic), PER (peritoneum), BRA (brain), ADR (adrenals), LYM (lymph nodes), SKI (skin), and OTH (others).

Positive results of peritoneal cytology, which are described as "Pcy1", should not be treated as distant metastases.

3.2.11.8 Stage Grouping of the Distal Bile Duct Cancers (Table 3.9)

The Japanese classification system is composed of a seven-stage grouping that utilizes the TNM factors. It is different from the UICC classification because the T4 tumour is classified as Stage IVA, distinct from M1 in the Japanese classification.

3.2.12 Records of Surgical Procedures for the Distal Bile Duct Cancers

3.2.12.1 Surgical Procedures

The procedures that can be performed for distal bile duct cancers are listed below. The record should be accompanied by information about the performance of cholecystectomy and procedures for reconstruction.

Bile duct resection
PD: pancreatoduodenectomy
PPPD: pylorus-preserving PD
SSPPD: subtotal stomach-preserving PD
Palliative surgery for biliary decompression
Bypass surgery of alimentary tract
Exploratory laparotomy and laparoscopy
Concomitant resections of neighbouring organs

Table 3.9 Stage grouping of the distal bile duct cancer (reprint from [5])

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage IIIA	T3	N0	M0
Stage IIIB	T1, T2, T3	N1	M0
Stage IVA	T4	Any N	M0
Stage IVB	Any T	Any N	M1

3.2.12.2 Evaluation of Surgical Margins

After each radical surgery, surgical resection margins are evaluated as positive or negative. The localization of the microscopic involvement in ductal margins should be recorded per the following notations: m (intraepithelial), w (intramural and extraepithelial), and ex (extramural). For dissected margin status, the localization of the microscopic involvement should be recorded per the following notation: PV (portal vein), HA (hepatic artery), D (duodenum), etc.

Distal Bile Duct Margin

DMX: Involvement of the distal bile duct margin cannot be assessed
DM0: No involvement of the distal bile duct margin
DM1: Microscopic, but not macroscopic, involvement of the distal bile duct margin
DM2: Macroscopic and microscopic involvement of the distal bile duct margin

Proximal Bile Duct Margin

HMX: Involvement of the proximal bile duct margin cannot be assessed
HM0: No involvement of the proximal bile duct margin
HM1: Microscopic, but not macroscopic, involvement of the proximal bile duct margin
HM2: Macroscopic and microscopic involvement of the proximal bile duct margin

Dissected Margin

EMX: Involvement of the dissected margin cannot be assessed
EM0: No involvement of the dissected margin
EM1: Microscopic, but not macroscopic, involvement of the dissected margin
EM2: Macroscopic and microscopic involvement of the dissected margin

Evaluation of Histologic Vascular Involvement

Location of the invaded portal or arterial system, or both, and the depth of invasion, such as

the adventitia (a), tunica media (m), and tunica intima (i), should be recorded.

Portal System Invasion Classified as T3 or T4

PVX: Histologic portal system invasion cannot be assessed
PV0: No histologic portal system invasion
PV1: Histologic portal system invasion

Arterial System Invasion Classified as T3 or T4

AX: Histologic arterial system invasion cannot be assessed
A0: No histologic arterial system invasion observed
A1: Histologic arterial system invasion observed

3.2.12.3 Evaluation of the Residual Tumours

After resecting the tumour, the condition of the macroscopic and pathological residues of the tumour is recorded. If the presence of carcinoma in situ is microscopically proven, it should be recorded as R1cis.

R0: No residual tumour
R1: Microscopic residual tumour
R2: Macroscopic residual tumour

3.2.13 Description of Primary Tumours of the Papilla of Vater

3.2.13.1 Tumour Location

Carcinomas of the ampullary region are defined as tumours arising in the ampullary region as shown in Fig. 3.8. If it is not possible to determine the exact site of origin, tumours are assumed to be carcinomas of the ampullary region if the bulk of the tumours are present in this region.

If more than one anatomical region is involved, all involved regions should be recorded in the order of involvement, starting with the region in which the bulk of tumour is located (e.g. AcbBd). The distinct location of the primary site should be underlined.

3.2.13.2 Size and Number of Lesions

The two greatest dimensions should be recorded for each lesion. In resected specimens, the number of tumours and the two greatest dimensions for each lesion should be recorded after opening the papilla of Vater.

3.2.13.3 Macroscopic Types

Gross tumour morphology is categorized based on either radiologic or pathological findings. Macroscopic types of primary tumours are classified per the appearance of the tumours viewed from the duodenal lumen and the growth patterns viewed from the duodenal wall (Table 3.10, Fig. 3.13).

3.2.13.4 Contiguous Extent of the Primary Tumour of the Papilla of Vater (T-Category)

The contiguous extent of the primary tumour is recorded as the T-category. Conventional characters denoting the depth of invasion (M, OD) may be appended.

Table 3.10 Macroscopic types of carcinoma of the ampullary region (reprint from [5], revised)

Protruded type	Tumours with a prominent intraluminal growth and without ulceration[a]
Mixed type	Ulcerated tumours without distinct elevation. Normal mucosa surrounds the margin of ulceration
Ulcerative	Tumours showing a coexistence of the protruded type and ulcerative type. This type of tumour is subdivided into the protruded-predominant and ulcerative-predominant types. Ulcerative tumours with raised margins, which suggest cancer invasion beyond the margin of ulceration, are included in the ulcerative predominant type
Others	Tumours that cannot be classified into any of the above types. Normal appearance, a polyp type or a unique type can be classified in this category

The protruded type is subdivided into the non-exposed protruded and exposed protruded types. Tumours with exposed protruded type can be observed from the duodenal lumen, while tumours with non-exposed protruded type are covered with mucosa of the duodenal papilla and cannot be seen from the duodenal lumen

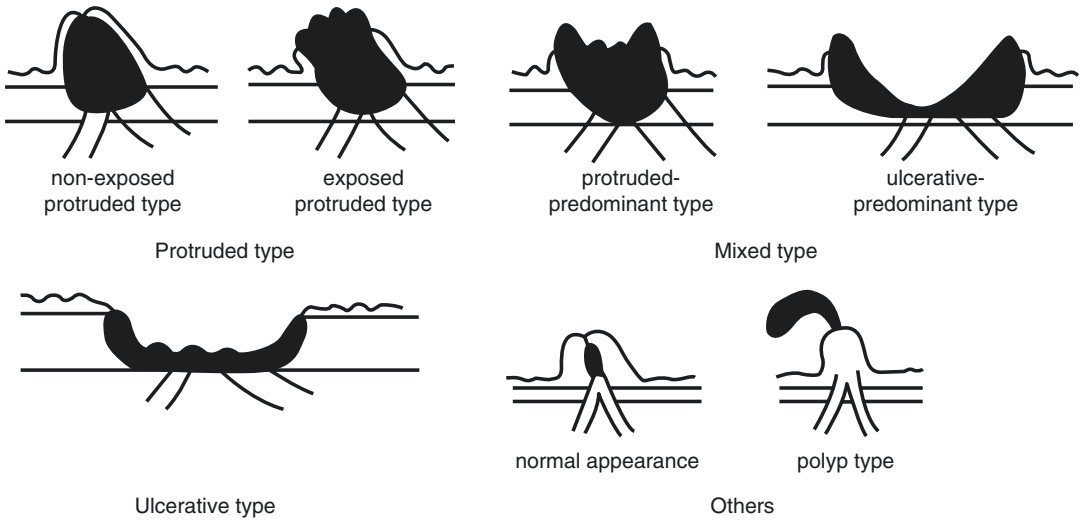

Fig. 3.13 The macroscopic types of tumours arising in the papilla of Vater (reprint from [5]). Macroscopic types are classified per the appearance of the tumours viewed from the duodenal lumen and the growth patterns viewed from the duodenal wall

Tx: Primary tumour cannot be assessed
T0: No evidence of primary tumour
Tis: Carcinoma in situ
T1a: Tumour confined to the mucosa
T1b: Tumour limited to the sphincter of Oddi
T2: Tumour invades the duodenal wall
T3a: Tumour invades the pancreas within 5 mm depth
T3b: Tumour invades the pancreas beyond 5 mm depth
T4: Tumour invades the peripancreatic soft tissues or other adjacent organs or structures

3.2.13.5 Description of Lymph Node Metastasis (N-Category)

In cancers of the papilla of Vater, the regional lymph nodes are the nodes on the posterior surface of the head of the pancreas (13a, b), the anterior surface of the head of the pancreas (17a, b), at the root of the mesenteric artery (14p, d), on the posterior and the right side surfaces of the bile duct in the hepatoduodenal ligament (12b), along the common hepatic artery (8a, p), and the supra- and infra-pyloric nodes (5, 6). It is not mandatory to dissect the nodes 5 or 6 or both (Fig. 3.14). The spread of cancers to lymph nodes other than regional lymph nodes are considered distant metastases (M1). The number of metastatic nodes and the rate of the total number of dissected nodes should be recorded in each station.

Nx: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastasis
N1: Regional lymph node metastasis

3.2.13.6 Description of Distant Metastasis (M-Category)

Metastases to distant organs and to lymph nodes other than the regional lymph nodes are considered distant metastases.

M0: No distant metastasis
M1: With distant metastasis

The category M1 may be further specified with the following notations: PUL (pulmonary), MAR (bone marrow), OSS (osseous), PLE (pleura), HEP (hepatic), PER (peritoneum), BRA (brain), ADR (adrenals), LYM (lymph nodes), SKI (skin), and OTH (others).

The positive results of peritoneal cytology which are described as “Pcy1” should not be treated as distant metastases.

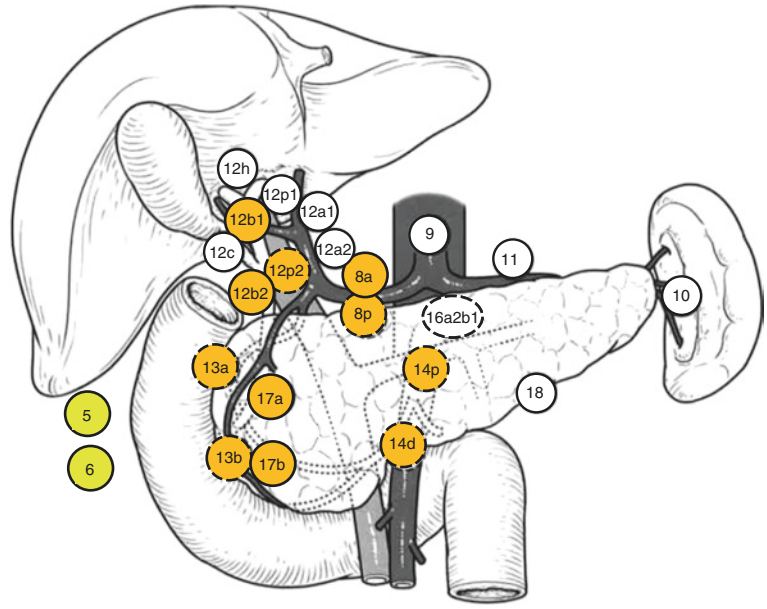

Fig. 3.14 The location and number of lymph node stations related to cancers of the papilla of Vater (reprint from [5], revised). The stations of regional lymph nodes of ampullary cancers are coloured in yellow. It is not mandatory to dissect the nodes 5 or 6 or both

3.2.13.7 Stage Grouping of Cancers of the Papilla of Vater (Table 3.11)

The Japanese classification system is composed of a seven-stage grouping, using TNM factors. It has similarities with the UICC classification.

Table 3.11 Stage grouping of cancer of the papilla of Vater (reprint from [5])

Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1, T2, T3	N1	M0
Stage III	T4	Any N	M0
Stage IV	Any T	Any N	M1

3.2.14 Records of Surgical Procedures for Cancers of the Papilla of Vater

3.2.14.1 Surgical Procedures

The procedures that could be performed for ampullary cancers are listed below. The record should be accompanied by information about the performance of cholecystectomy and procedures for reconstruction.

Endoscopic papillectomy
Transduodenal papillectomy
PD: pancreatoduodenectomy
PPPD: pylorus-preserving PD
SSPPD: subtotal stomach-preserving PD
Palliative surgery for biliary decompression
Bypass surgery of the alimentary tract
Exploratory laparotomy and laparoscopy
Concomitant resections of neighbouring organs

3.2.14.2 Evaluation of Surgical Margins

Margins of surgical resections are evaluated as positive or negative, after each radical surgery. Localization of the microscopic involvement in the proximal ductal margin should be recorded per the following notations: m (intraepithelial), w (intramural and extraepithelial), and ex (extramural). For the pancreatic stump margin, the localization of the microscopic involvement should be recorded per the following notations: d (intraductal) and p (pancreatic parenchyma). For the status of the dissected margin, the localization of the microscopic involvement should be recorded per the following notations: PV (portal vein), HA (hepatic artery), D (duodenum), etc.

Proximal Bile Duct Margin

HMX: Involvement of the proximal bile duct margin cannot be assessed
HM0: No involvement of the proximal bile duct margin
HM1: Microscopic, but not macroscopic, involvement of the proximal bile duct margin
HM2: Macroscopic and microscopic involvement of the proximal bile duct margin

Pancreatic Margin

PMX: Involvement of the pancreatic margin cannot be assessed
PM0: No involvement of the pancreatic margin
PM1: Microscopic, but not macroscopic, involvement of the pancreatic margin
PM2: Macroscopic and microscopic involvement of the pancreatic margin

Dissected Margin

EMX: Involvement of the dissected margin cannot be assessed
EM0: No involvement of the dissected margin
EM1: Microscopic, but not macroscopic, involvement of the dissected margin
EM2: Macroscopic and microscopic involvement of the dissected margin

3.2.14.3 Evaluation of the Residual Tumours

After resecting the tumour, the condition of macroscopic and pathological residue of the tumour is recorded. If the presence of carcinoma in situ is microscopically proved, it should be recorded as R1cis.

R0: No residual tumour
R1: Microscopic residual tumour
R2: Macroscopic residual tumour

3.2.15 Handling the Resected Specimens of the Cancers of the Distal Bile Duct and Papilla of Vater

3.2.15.1 Opening of the Duodenum and the Bile Duct (Fig. 3.15)

For a specimen obtained by pancreaticoduodenectomy, the posterior wall of the bile duct is opened from the cut end of the bile duct to the papilla of Vater. The duodenum is, in principle, opened along longitudinal direction to observe the papilla of Vater, the accessory papilla, and the mucosa of the duodenum. When the tumour is located around the confluence of the cystic duct or around the site in proximity to the common bile duct, the main pancreatic duct, and the accessory pancreatic duct, the bile duct may not be opened to assess the primary site and the extent of tumour spread.

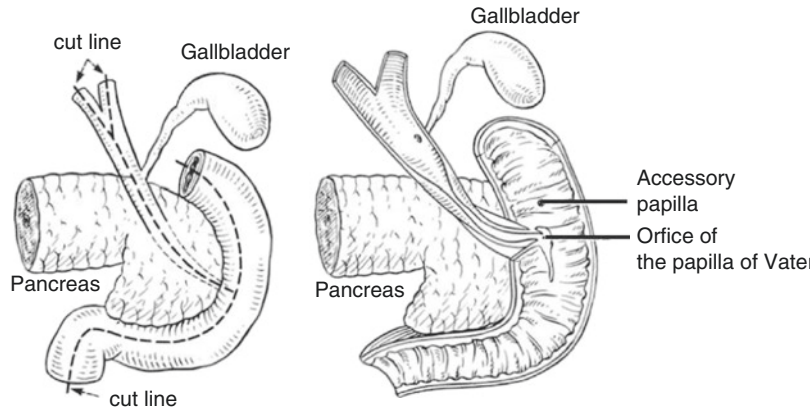

Fig. 3.15 The handling of specimens retrieved by pancreatoduodenectomy for cancers of the lower bile duct and the papilla of Vater (reprint from [5]). For a specimen obtained by pancreaticoduodenectomy, the posterior wall of the bile duct is opened from the cut end of the bile duct to the papilla of Vater. The duodenum is opened along the longitudinal direction

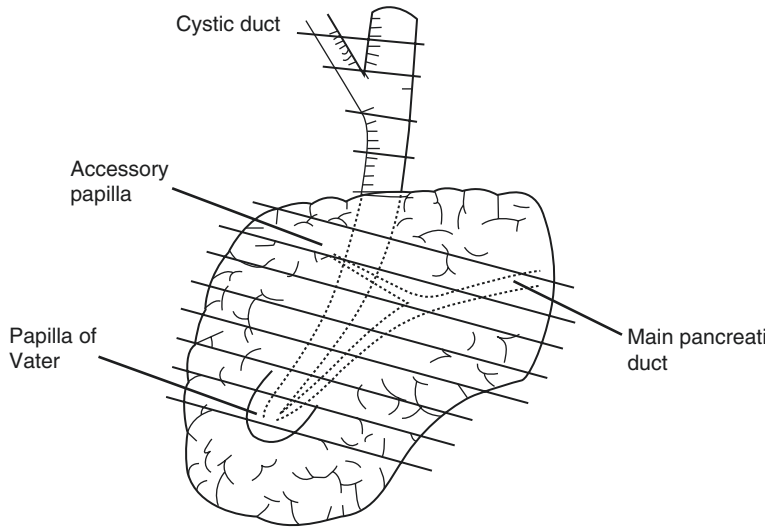

Fig. 3.16 Sectioning of the specimens of cancers of the lower bile duct and the papilla of Vater (reprint from [5]). The specimens obtained by pancreatoduodenectomy should be sectioned vertically along the longitudinal axis of the bile duct at 5-mm intervals

3.2.15.2 Sectioning of the Specimen

The specimen obtained by pancreatoduodenectomy should be sectioned vertically along the longitudinal axis of the bile duct at 5-mm intervals. The centre of the accessory papilla should be divided in each specimen (Fig. 3.16).

3.2.16 Histopathological Classification of Biliary Tract Cancers

The histological types of biliary tract tumours are shown in Table 3.12. If an epithelial tumour comprises more than one histological type, the predominant histological pattern should be adopted as the representative histological type.

Histological findings are further classified based on criteria such as "cancer stromal volume", "infiltrative pattern", and "lymph-vascular and (peri-)neural invasions".

3.2.16.1 Cancer Stromal Volume

Medullary type (med): Scanty stroma

Scirrhous type (sci): Abundant stroma

Intermediate type (int): The quantity of stroma is intermediate between the two above types

Table 3.12 Histologic types of biliary tract tumours and their abbreviations (reprint from [5])

(A) Adenocarcinoma
(1) Papillary adenocarcinoma (pap)
(2) Tubular adenocarcinoma
(i) Well differentiated (tub1)
(ii) Moderately differentiated (tub2)
(3) Poorly differentiated adenocarcinoma
(i) Solid type (por1)
(ii) Non-solid type (por2)
(4) Mucinous adenocarcinoma (muc)
(5) Signet-ring cell carcinoma (sig)
(B) Adenosquamous (cell) carcinoma (asc)
(C) Squamous cell carcinoma (scc)
(D) Undifferentiated carcinoma (ud)
(E) Choriocarcinoma (cc)
(F) Carcinosarcoma (cs)
(G) α-Fetoprotein-producing adenocarcinoma
(H) Neuroendocrine neoplasm (NEN)
(1) Neuroendocrine tumour (NET)
(i) NET G1 (carcinoid)
(ii) NET G2
(2) Neuroendocrine carcinoma (NEC)
(i) Large cell NEC
(ii) Small cell NEC
(3) Mixed adenoendocrine carcinoma (MANEC)
(4) Goblet cell carcinoid
(5) Tubular carcinoid
(I) Mucinous cystic neoplasm (MCN)
(J) Unclassified tumours (UCT)

3.2.16.2 Cancer Infiltrative (INF) Pattern into the Surrounding Tissues

INFa: The tumour shows an expanding growth pattern with a distinct border from the surrounding tissues
INFb: The tumour shows a growth pattern that is intermediate between INFa and INFc
INFc: The tumour shows an infiltrating growth pattern with an indistinct border from the surrounding tissues

3.2.16.3 Lymphatic Invasion

ly0: No lymphatic invasion
ly1: Minimal lymphatic invasion
ly2: Moderate lymphatic invasion
ly3: Marked lymphatic invasion

3.2.17 Venous Invasion

v0: No venous invasion
v1: Minimal venous invasion
v2: Moderate venous invasion
v3: Marked venous invasion

3.2.17.1 (Peri)Neural Invasion

ne0: No (peri)neural invasion
ne1: Minimal (peri)neural invasion
ne2: Moderate (peri)neural invasion
ne3: Marked (peri)neural invasion

3.2.18 Precursor Lesions of Biliary Tract Cancers

Two types of precursor lesions have been proposed for the development and progression of extrahepatic bile duct cancers and gallbladder carcinomas: intraluminal papillary neoplasms of the biliary tract (IPNB) and biliary intraepithelial neoplasia (BilIN).

These neoplasms display a spectrum from premalignant lesions to invasive carcinomas. Intraluminal papillary neoplasms showing carcinomas in situ and invasive carcinomas correspond to the papillary type of extrahepatic bile duct cancers, as defined in this manual. BilINs are further classified into BilIN-1, BilIN-2, and BilIN-3 based on the degree of cellular and nuclear atypia. BilIN-3 corresponds to carcinomas in situ.

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4 Imaging Evaluation of Resectability

Ashish Verma

4.1 Introduction

Periampullary region of the anterior pararenal space of the retroperitoneum houses the pancreatic head and uncus, lower part of the common bile duct, ampulla of Vater, and the adjacent duodenum. Neoplasias arising from each of these have to be managed in a different way and carry radically different prognoses [1]. The focus of preoperative imaging evaluation hence remains on segregating pancreatic tumors, especially adenocarcinoma, from other periampullary cancers. An imaging-based subclassification of lesion histomorphology followed by mapping of the spleno-mesentric-portal and aorto-mesenteric vascular structures forms the basis of decision about the resectability of periampullary tumors [2]. Multi-detector computed tomography (MDCT) is the most suitable tool for evaluation of the said features, while magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS) may be resorted to under specific circumstances, viz., evaluation of complex and cystic lesions [3]. A reasonable understanding of the imaging technology for a surgeon forms the basis of further evaluation and understanding of imaging results [4, 5].

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4.2 Technical and Technological Aspects

4.2.1 The Pancreatic Protocol CT Scan [6–8]

A "pancreatic protocol CT scan" remains the basis for rational imaging evaluation of pancreatic and periampullary cancers in current practice [9]. Though the patient is exposed to an additional dose of radiation, the method offers a definite advantage over the conventional scanning technique not only in vascular mapping but also while characterization of lesions. The volume data generated by present day multislice CT scanner is isotropic hence reconstructions as thin as 0.1 mm in all possible anatomical planes. There is no loss of anatomical details or distortion of image morphology in this multiplanar reconstruction (MPR) [10]. Further the vascular anatomy and relation of the pathology to the same can be depicted in three-dimensional volume reconstruction which may give a surgeon a more lucid impression of the operative field. The third and most important advantage offered by the "pancreatic protocol scan" lies in the capability to image whole of the organ multiple times in a single breath-hold. This enables evaluation of the pattern of blood flow as a function of time within the pathology as well as the normal structures in the field. The evaluation of dynamic enhancement pattern of tumor is quite helpful in

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characterization of the pathology, as this is utilized as a surrogate of tumoral neoangiogenesis. The protocol consists of a "pancreatic phase" acquired at 30–40 s after intravenous injection. This phase is most sensitive for initial diagnosis as well as for characterization of lesion within the pancreatic parenchyma, most of which remain equivocal in the pure arterial phase (15–30 s) and the portal venous phase (45 s). The field of view [FOV] in the "pancreatic phase" scanning is limited and is aimed at imaging the pancreatic fossa with a high spatial resolution. The pancreas derives arterial feeders from the splenic artery which in turn is a branch of the celiac trunk, wash-in of iodinated contrast media in the pancreatic parenchyma occurs slightly late as compared to other major organs which derive a direct aortic arterial supply, and the "pancreatic phase" is designed to achieve an optimum trade-off between a pure arterial and the venous phases [11, 12]. The biology of pancreatic tumors renders them a relatively hypo-vascular state (in early phase) in comparison to the native parenchyma of the gland due to the fact that most such lesions derive arterial supply from the pancreatic arteries. The preferential channelization of arterial flow toward native parenchyma, preceding the tumoral supply, results in a significant and diagnostic contrast difference between the two (the contrary being visible in the portal venous phase when the tumor shows more enhancement than the native gland). Second to the "pancreatic phase," a "portal venous phase" with extended field of view for detection hepatic metastases and as well as nodal involvement is taken. Further scanning in "portal venous phase" also helps in evaluation of other periampullary tumors [12]. Negative oral contrast may be administered to assist in the latter exercise as the same makes the wall of the bowel more conspicuous and distended [13]. The phasing of intravenous contrast injection is enabled by pre-synchronization of image acquisition protocol to an automated power injection system for delivery of intravenous contrast. The same is achieved either by a "test bolus" or a "smart prep" technique. Intravenous iodinated contrast media is injected optimized to body weight and surface area is injected at a rate of 4 mI/sec into an antecubital vein and scanning performed at 15–20, 35–40, and 65 s with a 3-mm collimation. A delayed phase (at 120 s) may also be included to differentiate hepatic hemangiomas from metastases, not an uncommon scenario in everyday practice [14].

4.2.2 Role of Other Advanced Diagnostic Techniques

Magnetic resonance imaging (MRI) has been utilized as the second-line modality to address certain queries that remain unattended on CT scan. Protocol similar to above can be planned for MRI as well using intravenous gadolinium injection and three-dimensional image acquisition. The modality offers superior contrast resolution than CT scan but suffers the disadvantage of having a poor spatial resolution [15, 16]. Further even in the developed world, the modality has a limited availability and high cost factor. The main indications are in patients of compromised renal function and in those where preoperative characterization of a tumor is important for surgical planning. In our experience a T1-weighted fat-suppressed MRI offers significant gain in sensitivity over contrast-enhanced CT due to the inherent natural contrast of a tumor from the native tissue [17]. *Endoscopic retrograde cholangiopancreatogram (ERCP)* has been classically utilized to evaluate the obstruction of the biliary tree caused by periampullary cancers. MRI sequence with a high T2 weighting known as *magnetic resonance cholangiopancreatogram (MRCP)* has superseded ERCP for this purpose, and the latter is now utilized only in situations where a preoperative endoscopic biliary bypass stenting has been planned. The "duct penetration sign" on MRCP, to differentiate inflammatory from neoplastic pancreatic mass, can be correlated better with axial images obtained on MRI. The advent of MRCP has obviated the need of ERCP for pure diagnostic purpose, hence reducing the incidence of procedure-associated morbidity, complications of injecting iodinated contrast in the bile ducts, and the radiation

risks. *Positron emission computed tomography (PET-CT)* is a staging technique in current practice performed as an adjunct to either of the above for detection of metastases and nodal involvement. The exquisite sensitivity of PET combined with anatomical mapping enabled by CT scan makes PET-CT the modality of choice for this purpose. High-grade neoplasias are "avid" for the uptake of biometabolites like 18-fluorodeoxyglucose (FDG) which may not be taken up as briskly and voluminously by benign lesions and inflammatory lesions. PET performs better than most other modalities (performed in isolation or in combination) for detection of distant metastases with the sensitivity and specificity approaching 100%. *Endoscopic ultrasound (EUS)* has been reserved for evaluation of equivocal cystic tumors and for performing EUS-guided fine-needle aspiration (EUS-FNA). EUS-FNA offers a sensitivity of 80–95% for the initial diagnosis of pancreatic malignancies with obstructive jaundice and chronic pancreatitis adversely affecting the accuracy. Local staging is achieved with an accuracy of 78–94%, while accuracy for nodal involvement is 64–82%. Endoscopic sonography for pancreatic lesions however suffers from a significant inter-observer and intra-observer variations in interpretations due to a high reliance on operator capabilities and expertise. Further the semi-invasive nature of EUS and invasive aspect of EUS-FNA render a risk of certain complications in 0.1–1% cases, viz., hemorrhage, perforation, complications related to anesthesia, and chances of pancreatitis [18]. *Diagnostic laparoscopy* offers a significant gain in sensitivity for detection of fine peritoneal surface metastases and hepatic metastases. *Contrast-enhanced ultrasound (CEU)* however offers challenge to the former for evaluation of fine metastases in solid organs. With the availability of safe intravenous microbubble sonographic contrast media, CEU has been integrated in routine protocol in high-volume centers where stringent preoperative confirmation of all aspects is mandated to justify the waiting lists for surgical procedure. Staging laparoscopy with laparoscopic ultrasound however remains the modality of choice to study the peritoneal lesions. Indications for staging laparoscopy being an index lesion of more than 3 cm, an elevated CA 19-9 level (>1000 U/mL), and/or persistent dilemmas on CT scan. In the presence of these findings, the incidence of laparoscopic findings altering management is >10% [19].

4.3 Imaging Appearances of Pancreatic and Periampullary Tumors

Resectability criteria of pancreatic and periampullary tumors are adjudged primarily on the basis of imaging, especially "pancreatic protocol CT scan." Further, characterization of tumors enables an evidence-based approach in deciding the treatment protocol. The exercise of imaging of such tumors consists of three steps as elaborated below.

4.3.1 Initial Detection and Characterization [20]

Adenocarcinoma of the pancreas (Fig. 4.1) is the most common neoplasia causing distortion of pancreatic anatomy and occurs most of the time in the head region (90–95%). The tumor shows less wash-in of contrast media than the native pancreatic parenchyma in the pancreatic phase of CT scan. Locoregional invasion and adenopathy are the other primary signs that may help in detection and characterization of lesion in conjunction with CA 19-9 level estimations in serum [21, 22]. The secondary signs which may assist in detection of an inconspicuous tumor include an upstream pancreatic and biliary ductal dilatation with a "sharp cutoff" at the mass [23–25]. Numerous fine non-enhancing cysts which mostly remain imperceptible on imaging characterize the *serous cystic pancreatic tumors* [26]. Brisk enhancement of septations within the lesion in the pancreatic parenchymal phase may be noted along with a delayed enhancing central fibrous stellate scar having "sunburst" calcification. Portal phase CT scan usually reveals a "honeycomb" appearance, but a solid-looking lesion

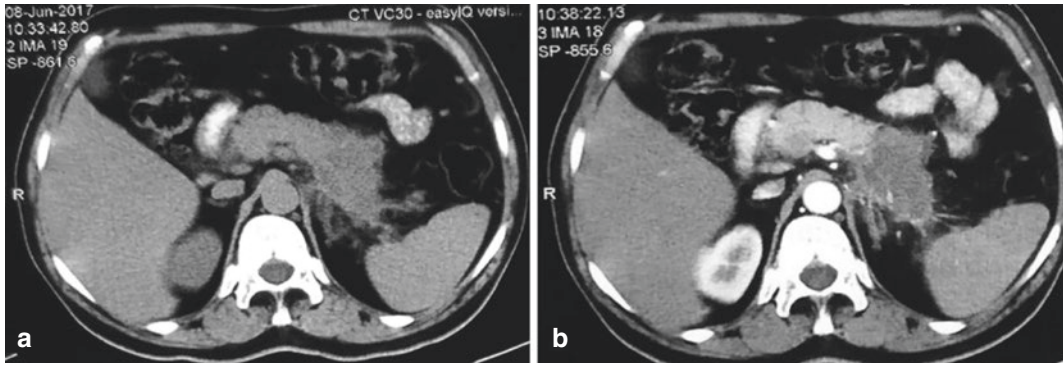

Fig. 4.1 (**a**) Non-contrast and (**b**) contrast-enhanced CT scan showing a typical pancreatic adenocarcinoma in the body of pancreas with exfiltration to adjacent fat and fascial planes. The splenic vessels are encased while the lesion is extending and involving the left diaphragmatic crura

is also not uncommon. Rarely internal hemorrhages may be characterized well on MRI, and even certain fluid levels may be seen due to evolution of the sanguineous component of such cysts [27]. These lesions are mostly located in the head of the pancreas and are rarely if ever invasive in nature. Pancreato-biliary ductal dilatation may however be not uncommonly seen, but communication with ducts is almost never visualized [28, 29]. The *mucinous cystic tumors* comprising of *intraductal papillary mucinous tumors (IPMN)* (Fig. 4.2) *and mucinous cystic neoplasms (MCN)* (Fig. 4.3) have larger (>20 mm) but fewer (usually <6) cysts. Since these lesions arise from the pancreatic duct epithelium, focal pancreatic duct dilatation is noted commonly in both tumors [30, 31]. The zone of origin of an IPMN is in proximity to the major ducts and the ampulla of Vater than an MCN; hence, macroscopic ductal communication is more commonly seen in IPMN than in MCN [32, 33]. Accordingly an IPMN may be classified as main duct variety, side branch variety (mostly in head and uncinate process), and combination; they may also be classified as diffuse or segmental, based on the extent of involvement [34]. As the lesion enlarges, adjacent pancreatic parenchyma is compressed to form a "pseudocapsule"; further a fallacious appearance of "internal septations" may be seen due to conglomeration of dilated ducts which may mimic a serous cystic tumor [35]. The presence of pancreatic atrophy, absence of calcification, poor enhancement of the misrepresented "septae" in all phases, and occurrence of the lesion in older men are some of the features favoring a diagnosis of IPMN [36, 37]. In advanced cases excess mucin secreted by the tumor not only fills up the duct but also extrudes through the ampulla of Vater giving a "fish eye" appearance on endoscopy, EUS, and MRI. The relation of the mucinous cystic tumors to the ductal system is well depicted on MRCP, while a possible malignant transformation may be suggested by the presence of an intralesional enhancing nodule or a thick septa, best seen on contrast-enhanced fat-suppressed T1W MRI [38]. The shift toward malignant end of spectrum is more common with MCN. Exophytic location and mural calcification though uncommon overall may be encountered in MCN (than IPMN). Hepatic metastasis may be present in malignant MCN hence a delayed phase imaging is of importance in these patients. As we notice from the above discussion, cystic tumors of the pancreas may rightly be divided into unilocular cysts (MCN, IPMN, oligocystic serous cystadenoma, lymphoepithelial cyst, and cystic pancreatic NET), microcystic lesion (serous cystadenoma), macrocystic lesions (MCN, IPMN, and lymphoepithelial cyst), and cysts with solid components (malignant MCN, IPMN, cystic pancreatic neuroendocrine tumor, solid papillary neoplasm, adenocarcinoma) based on image morphology [39–43].

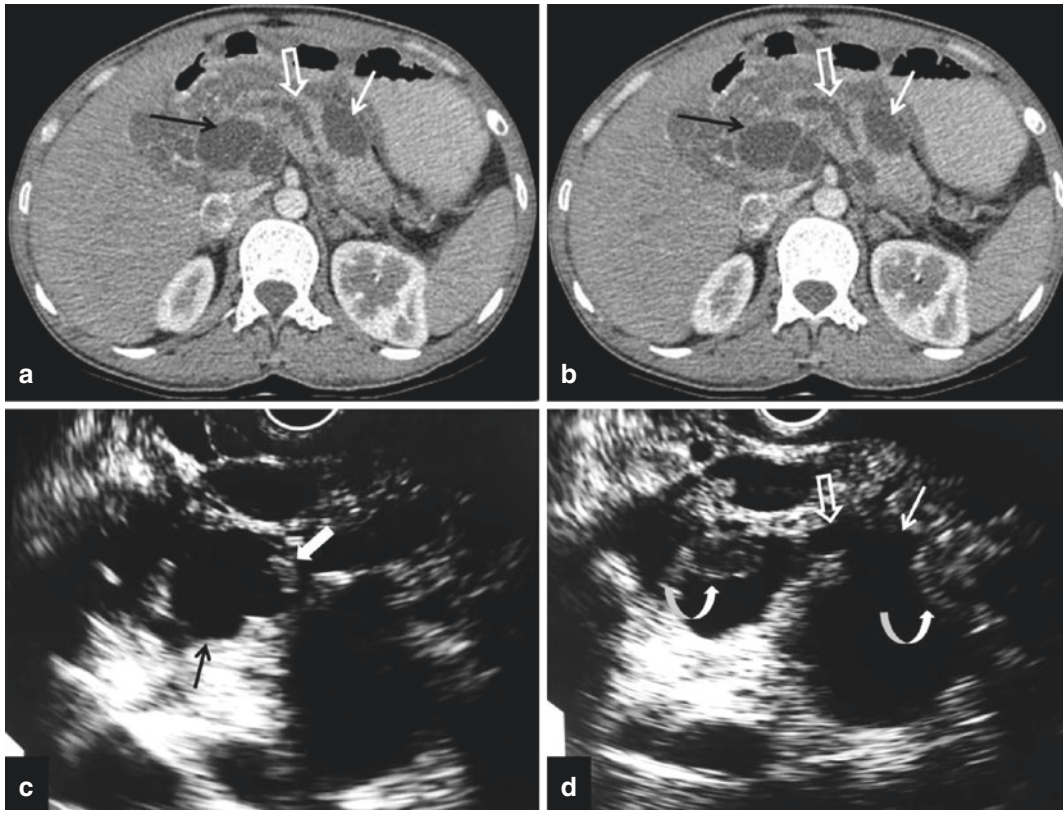

Fig. 4.2 (**a**, **b**) Contrast enhanced CT scan showing multiple cystic lesions (straight arrows) through out the pancreas with a dilated pancreatic duct (open arrow). (**c**, **d**) Endoscopic sonography shows intraductal mural nodules (curved arrows in **d** and solid arrow in **c**) with ductal communication with one of the cysts (open arrow in **d**) confirming the possibility of IPMN

The *neuroendocrine tumors (NET) of the pancreas* [44–46] are tumors which are rare and locally docile but have a definite metastatic potential notably to the liver. The functional tumors secrete hormones and cause specific clinical syndromes [47, 48]. The nomenclature of these lesions are according to the bioactive metabolite secreted or detected on special pathological techniques as 30–40% of such lesions are nonfunctional [49, 50]. An association with inherited genetic syndromes like MEN-1 and VHL disease should be ruled out especially when synchronous extrapancreatic tumors or multiple NET in the pancreas are seen [51]. The arterial phase of MDCT or the pancreatic parenchymal phase forms the basis of detection and characterization of these tumors and their metastases as they show brisk early enhancement and wash-out till the venous phase. EUS may be utilized to sample the lesion by fine needle in equivocal cases. Another situation where EUS may be of importance includes location of these tumors, especially gastrinoma, within the bowel wall. A comprehensive imaging protocol as described earlier in this text should be followed to detect local invasion and metastases to the liver, adrenals, lymph nodes, bones, and lungs. *Solid pseudopapillary neoplasm (SPEN/SPT)* (Fig. 4.4) is a bulky tumor with late enhancement and low malignant potential. The appearance on imaging is heterogeneous due to hemorrhagic tendency of these lesions [34, 52–56]. The pancreas is one of the common organs for seeding of *hematogenous metastases and non-Hodgkin lymphoma*, both of which may present as multifocal mass lesions showing less

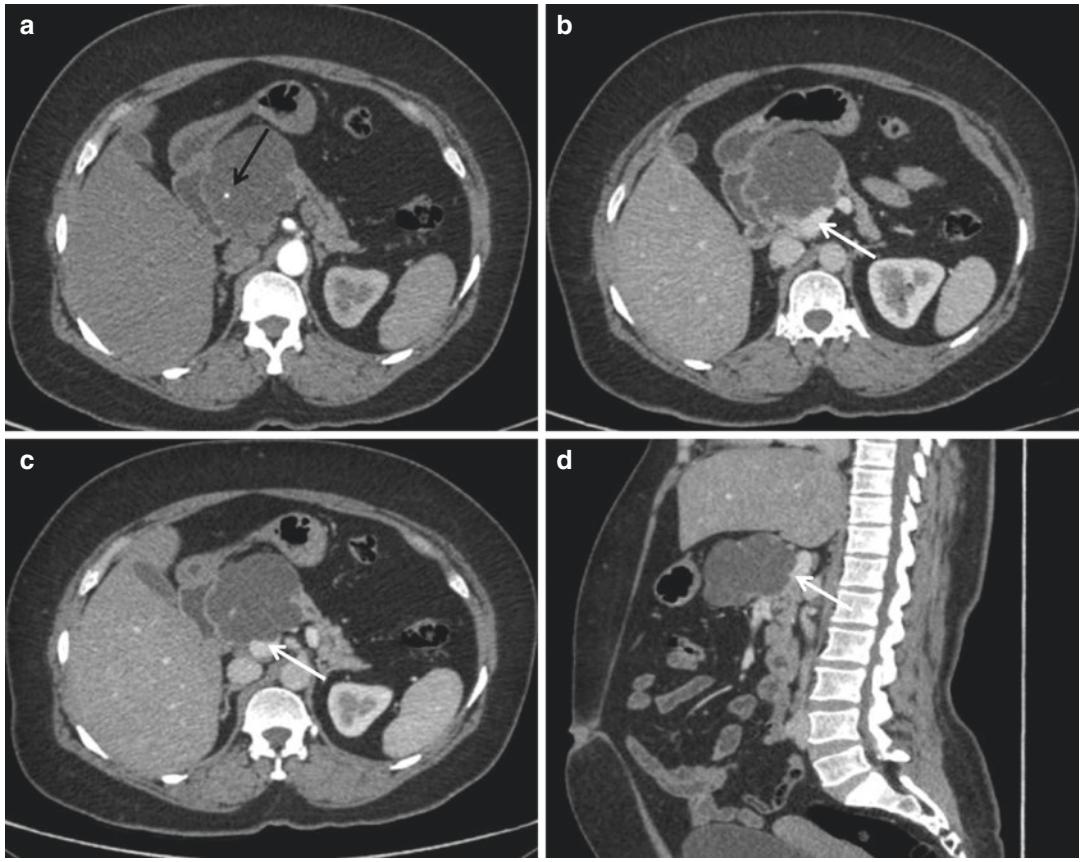

Fig. 4.3 Contrast enhanced CT scan in a case of mucinous cystic tumor in head of pancreas. Note the clear cut margin with portal vein in spite of close abutment (straight white arrow in panel **b**–**d**). Calcified septa may (straight black arrow in panel **a**) may be seen within the lesion

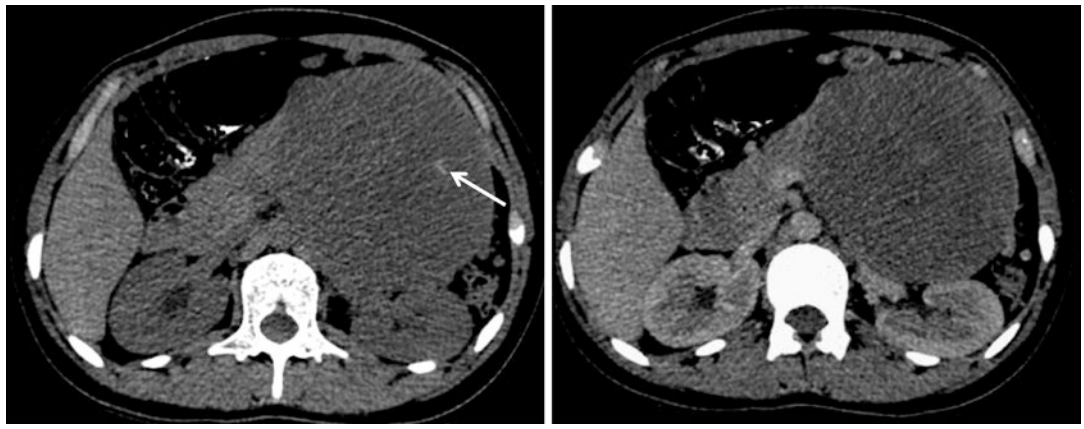

Fig. 4.4 Non-contrast (left panel) and Contrast-enhanced (right panel) C.T scan showing a typical SPEN. Note the bulky yet well defined and predominantly solid nature of lesion with a speck of calcification (straight arrow)

enhancement than the native parenchyma in the pancreatic phase of CT scan or MRI and a delayed enhancement thereby [57]. Diffuse pancreatic enlargement mimicking pancreatitis is another presentation of these lesions; the absence of telltale signs of retroperitoneal inflammation may assist in imaging diagnosis of these tumors [58, 59]. *Primary pancreatic squamous cell carcinoma* is a rare diagnosis of exclusion with no specific imaging features [60–62].

As already specified, periampullary tumor is a generic name allotted to a group of tumors based on their anatomical location. These include unrelated neoplastic pathologies like the *carcinoma of the ampulla of Vater, duodenal adenocarcinoma, duodenal gastrointestinal stromal tumors (GIST) and adenoma, and exfiltrating pancreaticoduodenal lymphadenopathy* [63, 64]. Most lesions show a poor early enhancement on a pancreatic protocol CT scan with delayed pooling of contrast. Variable locoregional infiltration is seen depending upon the grade of the primary tumor, but the presence of the "double duct sign" is common to all lesions due to obstruction of both the pancreatic and biliary ductal systems. Further imaging signs of bowel obstruction and loss of gut signature may also be seen. Notably the malignant villous adenomas of the duodenum show enhancement on the arterial phase CT scan with invasion of the pancreas [63, 64]. *Tubercular adenopathy* in this region and pancreatic tuberculosis are close mimickers of pancreatic and periampullary neoplasia and should always be kept as an imaging differential. EUS-guided fine-needle aspiration and functional imaging, like PET and diffusion-/perfusion-weighted MRI, may be of help in differentiating tuberculosis from a neoplastic pathology [65].

4.4 Preoperative Imaging Work-Up [17, 66]

Surgical planning for pancreatic cancers needs good quality imaging work-up to carefully assess the relation of tumor to the locoregional arteries and spleno-portal axes [67, 68]. The common anatomical variations of arterial system should also be mentioned in the summary of imaging observations as the same is important from the point of view of the kind of vascular reconstruction that might be required in a particular patient. The TNM-AJCC classification forms the basis of reporting template during work-up of pancreatic and periampullary cancers (Table 4.1). Involvement of commonly affected lymph node groups should also be notified; nodes which are anatomically distal to the gastroduodenal artery form poor prognostic indicators [69].

Macroscopic vessel involvement (Fig. 4.5) and the presence of metastasis are the most important determinants of long-term survival after surgery, which are optimally commented upon by imaging. The celiac trunk (CA), common hepatic artery (CHA), superior mesenteric artery (SMA) with first jejunal branch, and aorta should be evaluated for the circumferential contact with the tumor. A contact of <180° with sufficient stump available for reconstruction is a parameter favorable to the surgeon; this may however not hold good if significant contact to the aorta or the first jejunal branch is present. Extraluminal tumoral contact of up to 180° with the spleno-portal axes renders the lesion borderline resectable. MDCT can exclude resectability with a positive predictive value of 89–100% [70]. Multiplanar reconstruction directly perpendicular to the seam of vessels is important and should be routinely evaluated to

Table 4.1 Resectability criteria of pancreatic tumors in correlatin with staging

		CT scan—tumor-vessel relationship			
Clinical stage	AJCC stage	SMA	Celiac axis	CHA	SMV-PV
Resectable	I/II	Normal plane	Normal plane	Normal plane	Patent (± abutment/ encasement)
Borderline	III	Abutment	Encasement	Abutment or short segment encasement	± short segment occlusion, reconstructable
Locally advanced	III	Encasement	Encasement	Encased, non-reconstructable	Occluded, non-reconstructable

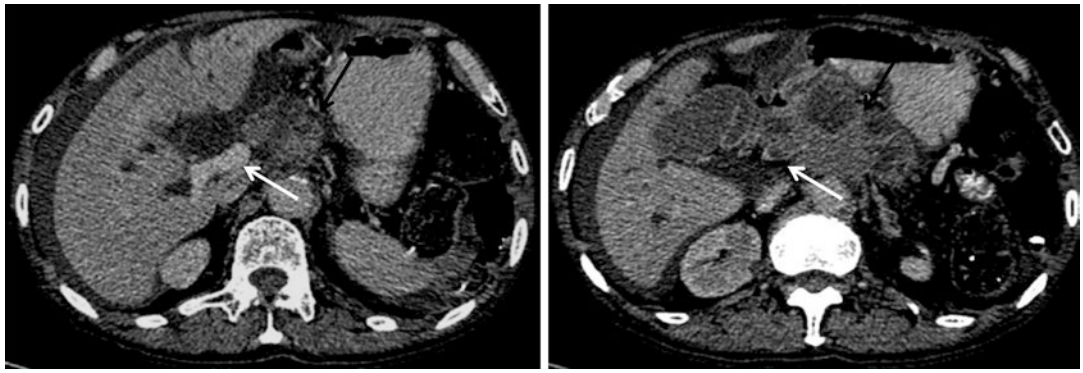

Fig. 4.5 Contrast enhanced CT scan showing a typical case of disseminated pancreatic adenocarcinoma. Note the portal vein and extension of a tumor thrombus within the vein lumen (straight arrow). The accompanying hepatic artery is non-visualized at the level due to complete involvement. Extension within vein is not an important consideration but arterial involvement may change the surgical planning

increase the level of confidence in subtle lesions [71]. Metastases are best evaluated by PET-CT; delayed phase of pancreatic protocol CT scan however may also detect hepatic metastases in a sizable number of cases [72].

The imaging evaluation of pancreatic and periampullary cancers begins with a good quality pancreatic protocol MDCT scan. The lesions in this region are closely located and complex in morphology; hence, assistance from other problem-solving modalities like MRI and endoscopic sonography may also be restored to in specific circumstances. The resectability criteria in current practice however largely depend on CT scan demonstrating tumoral proximity to the major vessels in the region, lymph nodal enlargement, and presence of metastases [73, 74]. Though tumor morphology is assessed mainly during the process of lesion characterization and initial diagnosis, certain cystic tumors and nonfunctional neuroendocrine tumors may be followed up biannually if diagnosed prospectively. This would not only prevent the morbidity associated with extended surgical procedures but also be cost accounting.

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5 Role of Preoperative Biliary Stenting and Preoperative Preparation Before Pancreaticoduodenectomy

Rishi Batra and Chandrakanth Are

5.1 Introduction

In the United States, an estimated 53,070 new patients will be diagnosed with pancreatic cancer in 2017, of which the majority is expected to die from the disease [1]. Nearly 85% of these exocrine pancreatic cancers will be adenocarcinomas for which surgical resection is the only potentially curative treatment option. The overall 5-year survival for pancreatic cancer is dismal at 6% [2]. After pancreaticoduodenectomy, the 5-year survival is about 25–30% for node-negative and 10% for node-positive disease [3, 4].

5.2 Biliary Stenting

Allen O. Whipple first described the need for biliary decompression in 1935 [5]. Until the late 1970s, management of malignant pancreatic and biliary obstruction in unresectable patients included surgical bypass with a choledochojejunostomy or hepaticojejunostomy. In 1974, percutaneous transhepatic cholangiography (PTC) was introduced with the use of a thin flexible 22-gauge needle (Chiba needle) by Kunio Okuda in Japan. Percutaneous transhepatic biliary decompression was initially reported to lower operative morbidity in patients with obstructive jaundice [6]. In 1980, Soehendra and Reynders-Frederix first described the use of endoscopic biliary stenting for decompression [7]. It has been noted by some that biliary drainage can combat the adverse effects of biliary obstruction and cholestasis such as direct hepatic injury, impaired immune function, cardiovascular, and renal dysfunction [8–10].

The role of preoperative biliary stenting has been debated extensively. Reduced mortality, less morbidity, and shorter hospital stays have been reported by some [11–14], while others have found no difference in outcomes in comparison to patients who went directly to surgery [15, 16]. Biliary stenting can be used as a bridge to surgery for pancreatic cancer [10] (to relieve jaundice and pruritus, minimize the risk of developing cholangitis, and also facilitate the administration of neoadjuvant therapy in patients with locally advanced pancreatic cancer) or for palliation in patients with unresectable disease.

A large Dutch study, DRainage vs. OPeration (DROP trial), evaluated the rate of serious complications for patients undergoing preoperative biliary drainage (PBD) for 4–6 weeks, followed by surgery, or to undergo surgery alone within 1 week after diagnosis [17, 18]. The rates of overall serious complications were significantly higher in patients who underwent PBD (74% vs. 39%, $p < 0.001$) compared to surgery alone. However,

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there was not a significantly increased rate of surgery-related complications (47% vs. 37%, $p = 0.14$). It was concluded that routine PBD in patients undergoing surgery for pancreatic cancer increased the rate of serious complications. Some of the high complications can be attributed to the small plastic stents used in the study [19]. Self-expanding metallic stents (SEMSs) have been shown to be superior in terms of durability and patency. Thus, metallic stents are now preferred and recommended over plastic stents whenever PBD is indicated [20, 21].

In the most recent Cochrane review (2012) of six trials with 520 patients comparing preoperative biliary drainage (265 patients) versus no preoperative biliary drainage (255 patients), it was concluded that there is currently not sufficient evidence to support or refute routine preoperative biliary drainage for patients with obstructive jaundice [22]. Preoperative biliary drainage did not reduce mortality in patients with obstructive jaundice. It was not recommended to routinely use preoperative biliary drainage in patients with obstructive jaundice who are about to undergo surgery outside well-designed randomized clinical trials.

5.2.1 Indications

Routine preoperative biliary stenting via endoscopic retrograde cholangiopancreatography (ERCP) remains controversial due to the risks associated with the procedure such as infection, pancreatitis, and bleeding. The major benefits of decompression remain relief of jaundice and to prevent complications due to cholestasis. The major indications for preoperative biliary drainage include acute cholangitis, intense pruritus, and when surgery is anticipated to be delayed for greater than 2 weeks [23] (Table 5.1, Fig. 5.1).

Table 5.1 Indications for biliary stenting

Acute cholangitis
Intense pruritus
Delayed surgery (>2 weeks)

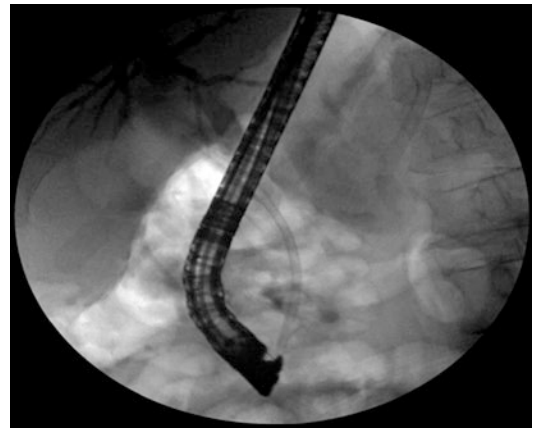

Fig. 5.1 ERCP-guided stent placement (Courtesy Shailender Singh, M.D.)

5.2.2 Types of Stents: Selection

Endoscopic biliary stenting has been reported to be technically successful in >90% of attempted cases [24]. Thus, relatively few require surgical biliary-enteric bypass as a planned palliative procedure. Plastic stents made of teflon, polyurethane, or polyethylene are inexpensive and effective and can be placed without sphincterotomy [10]. Stents typically measure 5–15 cm in length and include diameter sizes ranging from 7, 8.5, 10, to 11.5 Fr. However, plastic stents are more prone to develop occlusion by sludge and/or bacterial biofilm and are more likely to require repeated ERCPs. Plastic stent patency varies from 60 to 200 days. Self-expanding metallic stents are available as uncovered, partially covered, or fully covered. Metal stents were introduced to alleviate problems associated with plastic stents and extend the duration of stent patency [25, 26]. Initial concerns were raised that metallic foreign stents can incite inflammation and increase the difficulty or complexity of the surgical procedure. However, evidence has shown that metallic stents are safe and efficacious and can be used in the preoperative setting [27, 28] (Table 5.2).

Uncovered stents can be placed anywhere in the biliary tree but have limited removability and higher rates of tumor ingrowth [29, 30]. In contrast, the primary advantage of covered metal

Table 5.2 Types of stents

WallFlex stents (Boston Scientific)
Wallstent stents (Boston Scientific)
Zilver stent (Cook Endoscopy)
FLEXXUS stent (ConMed Corporation)
ALIMAXX-B stent (MeritMedical Systems, Inc.)
X-Suit NIR biliary stent (Olympus, Inc.)
Viabil stent (The W.L. Gore & Associates, Inc., marketed by ConMed Corporation)
Bonastent Biliary (EndoChoice, Inc.)

stents is the reduction of tumor ingrowth. Metallic stents can be made of stainless steel, nitinol (nickel and titanium), or Platinol. The benefits for metallic stenting include decreased rates of stent dysfunction, infectious complications such as cholangitis, and the need for re-intervention [10]. Mean patency rates of 278 days have been reported for metallic stents [31]. However, metal stents have higher costs and may not be extractable.

The most common complications associated with stenting include stent occlusion and stent migration. The rates of migration vary, however, approximately 5% of plastic stents and partially covered SEMSs are known to migrate. The highest rates of migration are noted in fully covered SEMSs that migrate at a rate of 20% [32]. Other, less common complications of biliary stent placement include pancreatitis, perforation, bleeding, infectious complications such as cholecystitis, and cholangitis [33]. The type of stent placed must be individualized to meet the needs of the patient (Fig. 5.2).

5.2.3 Tissue Diagnosis

Typically, histologic diagnosis is not required for patients with presumed pancreatic cancer when combined with appropriate imaging characteristics on high-quality pancreas protocol imaging. However, tissue biopsy is required prior to initiation of neoadjuvant therapy in patients with borderline resectable or locally advanced pancreatic cancer. Despite state of the art imaging, 20–33% of patients with presumed resectable disease were found to have unresectable disease intraoperatively [34–36]. Therefore, staging diagnostic laparoscopy is recommended in those with high likelihood of occult metastatic disease.

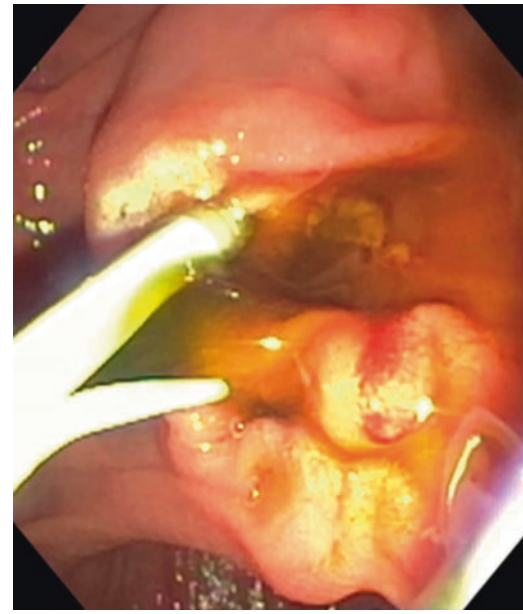

Fig. 5.2 Plastic stent placement (Courtesy Shailender Singh, M.D.)

5.3 Risk Stratification

Surgical resection remains the only potentially curative treatment option for the 15–20% of patients who are candidates for pancreatectomy. If resectability is technically feasible, the patient must be evaluated and risk stratified prior to undergoing a major noncardiac surgery. Initial preoperative evaluation of patient consists of a full history and physical examination to assess the risk for cardiovascular, pulmonary, or any other complication. Symptoms such as angina, dyspnea, syncope, and palpitations should be addressed. Any positive history of heart disease including ischemic, valvular, or myopathic disease should be explored to delineate disease severity, stability, and prior treatment [37]. A history of smoking, significant alcohol use, hypertension, diabetes, chronic kidney disease, and cerebrovascular or peripheral artery disease increases the risk of serious perioperative cardiac complication [38]. Key physical examination

findings may include cardiac murmur suspicious for heart failure and valvular heart disease. Cardiac functional status can be appreciated in terms of metabolic equivalents (1 MET is defined as 3.5 mL O_2 uptake/kg per min). The inability to climb two flights of stairs or walk four blocks is characterized as poor functional status and increases the risk of postoperative cardiopulmonary complications after major noncardiac surgery [37]. Daily smokers (>2 cigarettes a day for 1 year) have an increased risk of pulmonary and wound healing complications [39]. Patients that have a 20 pack-year smoking history have a higher incidence of postoperative pulmonary complication [40]. Smoking cessation 1 month prior to the operation is currently recommended to reduce associated risks [41]. Given the duration of the operation (>4 h), patients undergoing pancreaticoduodenectomy are at a higher risk of pulmonary complication [42, 43].

The risk for adverse cardiovascular event is related to patient-based risk factors and type of surgical operation. Proper identification and classification helps determine the potential morbidity and mortality associated with pursuing surgical intervention. The Revised Goldman Cardiac Risk Index estimates risk of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest based on the presence of any of the six independent predictors of major cardiac complications [44, 45] (Tables 5.3 and 5.4). Preoperative electrocardiogram (EKG) should be obtained to serve as a baseline for diagnosing potential abnormalities postoperatively.

Table 5.3 Revised Goldman Cardiac Risk Index (RCRI) [44]

High-risk type of surgery (examples include vascular surgery and any open intraperitoneal or intrathoracic procedures)
History of ischemic heart disease (history of MI or a positive exercise test, current complaint of chest pain considered to be secondary to myocardial ischemia, use of nitrate therapy, or ECG with pathological Q waves; do not count prior coronary revascularization procedure unless one of the other criteria for ischemic heart disease is present)
History of HF
History of cerebrovascular disease
Diabetes mellitus requiring treatment with insulin
Preoperative serum creatinine >2.0 mg/dL (177 μmol/L)

Table 5.4 Rate of cardiac death, nonfatal myocardial infarction, and nonfatal cardiac arrest according to the number of predictors [45]

No risk factors—0.4%
One risk factor—1.0%
Two risk factors—2.4%
Three or more risk factors—5.4%

5.3.1 Surgical Risk Calculator

The American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) has developed a decision-support tool based on 20 patient risk factors and multi-institutional clinical data which can be used to estimate the risks of most operations, including pancreaticoduodenectomy [46]. The ACS-NSQIP Surgical Risk Calculator estimates the likelihood of postoperative complications, including death after an operation. It also provides a predicted length of hospital stay tailored to the patient. The risk calculator may not capture every potential comorbidity; thus, surgeons may adjust the estimated risks within an interval if they feel the calculated risks are underestimated. The predicated risk of discharge to a nursing or rehabilitation facility can be provided to aid in preoperative planning and discussion with the patient and family. Using a predictive model is not always accurate but allows the surgeon to quantify the risks and potential complications associated with pursuing surgical intervention. Similarly, a preoperative nomogram was developed and is available to predict perioperative mortality following pancreatic resection for malignancy using common preoperative comorbidities [47].

5.4 Preoperative Preparation

Preoperative management of patients undergoing pancreaticoduodenectomy requires thorough assessment of medical conditions and nutritional

status. The patient must be optimized prior to surgery in an effort to reduce risk for postoperative complications and improve postoperative outcomes. A multidisciplinary treatment team consisting of surgeons, gastroenterologists, medical oncologists, radiation oncologists, and pain specialists can help deliver comprehensive care to patients in preparation for the operation. The thorough and complete treatment plan includes discharge planning, which begins prior to the operation.

After the patient has been risk stratified and appropriately evaluated for potential surgical intervention, the patient must be carefully counseled and perioperative expectations addressed. Surgeons have an ethical and legal duty to provide adequate information to the patient so that patients can make an informed decision on their treatment options [48]. Patients must understand their diagnosis, the proposed treatment or procedure, alternative treatment options (surgical or medical), risks and benefits of the treatment or procedure, and finally the risks of refusing treatment [49, 50]. The preoperative and postoperative expected course should be described, with an in-depth disclosure of potential complications that could occur, including death.

Nutritional support: Patients undergoing resection due to pancreatic cancer may become significantly malnourished and can rapidly develop anorexia-cachexia syndrome [51]. Greater than one third of patients with pancreatic cancer lose >10% of their initial body weight prior to diagnosis [52]. Weight loss may be due to ongoing symptoms of abdominal pain, anorexia, early satiety, nausea, vomiting, and diarrhea or constipation [53]. Additionally, metabolic aberrations may lead to increased protein catabolism and increased energy expenditure [54]. Although routine use of preoperative artificial nutrition is not warranted, significantly malnourished patients may benefit with oral supplements or enteral nutrition preoperatively. Seven to 10 days of preoperative parenteral nutritional support is recommended preoperatively for severely malnourished cancer patients.

Bowel preparation: Patients should be instructed begin a clear liquid diet beginning 48 h prior to scheduled resection. A study by Lavu et al. [54] noted no significant benefit for bowel preparation prior to pancreaticoduodenectomy. However, most surgeons still continue to use bowel preparation (mechanical or antibiotic or both) prior to pancreatic resection.

Thromboprophylaxis: The modified Caprini risk assessment model for venous thromboembolism (VTE) in general surgical patients estimates the risk of VTE [55]. Risk is further increased in patients with malignancy and in particular pancreatic adenocarcinoma [56]. Therefore, patients undergoing pancreaticoduodenectomy are considered to be moderate to high risk for VTE, and pharmacologic thromboprophylaxis is recommended in addition to intermittent pneumatic compression devices prior to induction of anesthesia. Venous thromboembolism was found to be decreased significantly when pharmacologic thromboprophylaxis was given to patients undergoing pancreatic resection for malignancy [57].

Discharge planning: Despite predictive models and risk assessment, it is difficult to determine disposition as postoperative morbidity determines the length of stay and the final discharge disposition. Pancreatic fistula, abscesses, and delayed gastric emptying are well-studied complications that can impede discharge to home [58]. Patients aged >70 years and those with three or more preoperative comorbidities are more likely to need assistance after discharge, and nearly half the patients will require some assistance after discharge [59, 60]. The home discharge rate was found to be decreased from 68.8 to 36.0% in patients aged >70 years. This becomes more important as the proportion of older patients with resectable pancreatic malignancies has also increased [61]. Therefore, discharge planning begins prior to the operation with a patient-centered approach.

5.5 Summary

Pancreatic resections are morbid procedures that are fraught with an acceptable mortality rate, but a high morbidity rate. A thorough, systematic, and methodical approach to preoperative planning and risk stratification is mandatory to improve patient selection and optimize outcomes.

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6 Pancreaticoduodenectomy for Cancer: Key Steps

Mallika Tewari

6.1 Introduction

Pancreatic and periampullary cancer is a dreaded disease with poor prognosis. Cancer affecting the pancreatic head and periampullary area is often treated by pancreaticoduodenectomy (PD), a technically demanding procedure of a deep-seated "active" gland. This is compounded by the fact that several arterial anomalies of the hepatic arterial system are often encountered [1]. The preceding chapters have illustrated the basic anatomy of the area and the gradual evolution of surgical resection of pancreatic/periampullary cancer. A triple-phase pancreatic protocol contrast-enhanced computed tomography (CECT) enables precise delineation of the pancreatic tumor and its relation with the surrounding structures and vessels, namely, superior mesenteric artery (SMA) and superior mesenteric vein (SMV), splenic vein (SV), celiac axis (CA), common hepatic artery (CHA), hepatic artery (HA) proper, gastroduodenal artery (GDA), portal vein (PV) and inferior vena cava (IVC), and aorta (AO). Various classification systems have evolved based on tumor-vessel interface (TVI) as seen on CECT segregating tumors as resectable, borderline resectable, and locally advanced/irresectable [2]. Over the years pancreatic cancer surgery has come a long way, and there has been a considerable drop in mortality (<1%) in high-volume centers though the morbidity still remains high (40%) [3, 4].

6.2 The Key Steps of Open PD

The operation "PD" is classically divided into six clearly defined steps to allow safe removal of the pancreatic head, duodenum, bile duct, and gallbladder ± distal stomach (Fig. 6.1a) [5–7]. These are (1) exposure of infrapancreatic SMV, (2) extended Kocher maneuver, (3) portal dissection, (4) stomach/pylorus/duodenum transection, (5) jejunal and ligament of Treitz transection, and (6) pancreas transection and uncinate dissection.

We follow the above steps though not exactly in the same sequence. Variations like SMA first approach and minimally invasive PD are altogether different techniques and are described in detail in separate subsequent chapters.

A diagnostic staging laparoscopy may precede a formal laparotomy in some institutions in patients with high risk for metastasis such as borderline resectable disease, those with markedly high serum CA 19-9 levels, large primary tumors, or large regional lymph nodes [2]. Intraoperative ultrasound can be used as a diagnostic adjunct during staging laparoscopy.

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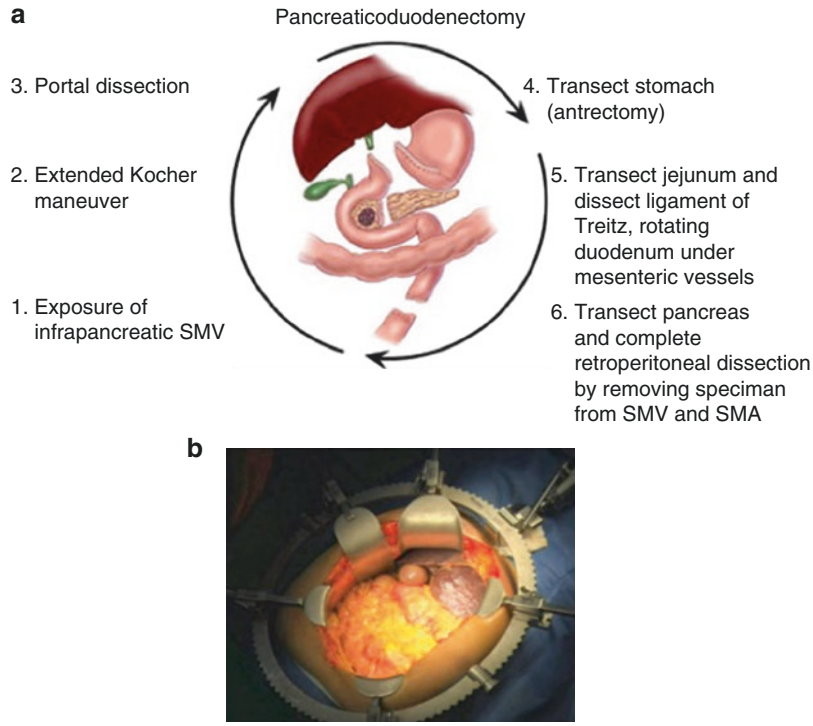

Fig. 6.1 (**a**) The classical six steps of pancreaticoduodenectomy. (**b**) Midline incision and good abdominal exposure with self-retaining abdominal retractor system

6.2.1 Exposure of the Infrapancreatic SMV

The abdomen is cleaned, draped, and opened by a midline incision. A bilateral subcostal incision is also used especially in large tumors requiring venous resection and reconstruction. We prefer a midline incision over the muscle cutting subcostal incision. The abdomen is then explored for any signs of metastatic disease. In a pancreatic head/periampullary cancer, the presence of large conglomerated lymph nodes at duodenojejunal (DJ) flexure is considered as highly suspicious for advanced disease and if present they are sent for frozen section for ruling out of metastatic cancer.

Abdominal wall self-retaining retractors are next positioned to ensure adequate exposure (Fig. 6.1b).

A large choice of modern abdominal retractor systems is now available such as Thompson, Omni-Tract, and Bookwalter Retractor Systems. They are table-mounted systems with retracting blades available in various shapes and when positioned give a good and stable retraction.

The omentum is lifted from over the transverse colon and the lesser sac is entered. The middle colic and right gastroepiploic veins are followed, and they guide to SMV that is then exposed at the inferior border of the pancreas (Fig. 6.2a). The SMV is covered by a thin layer of adventitial tissue, which is incised down to the plane of Leriche on the venous wall. The middle colic vein may drain separately or may join the right gastroepiploic vein. The right gastroepiploic vein together with superior colic vein and the anterior superior pancreaticoduodenal vein form the gastrocolic trunk of Henle that drains into the SMV. We prefer to leave the middle colic vein if it's draining separately and ligate the right gastroepiploic vein/gastrocolic trunk carefully between silk sutures as it drains into the SMV (Fig. 6.2b). There may be situations wherein the middle colic has to be ligated such as large

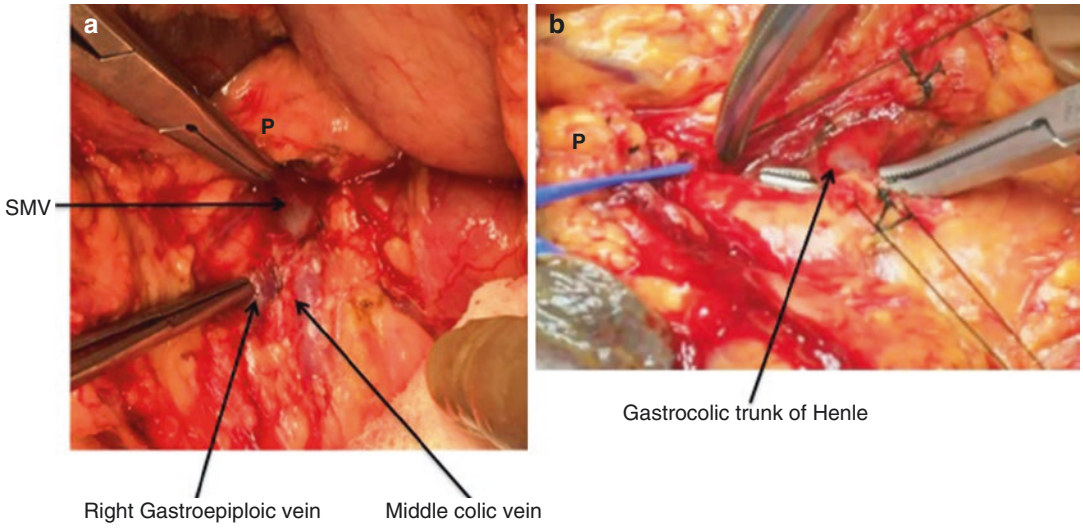

Fig. 6.2 (**a**) Identification of superior mesenteric vein (SMV) while tracing the right gastroepiploic and the middle colic vein through the lesser sac. (**b**) Ligation of the gastrocolic trunk of Henle

uncinate tumors and in obese patients. A plane is slowly developed over the SMV/PV in full vision till the upper border of the pancreas. Blind dissection is best avoided, as occasionally there might be a small stout vein draining in to the SMV/PV on its anterior surface. This step early in course of PD helps in assessment of the TVI and hence any need for venous resection of the SMV-PV confluence.

6.2.2 Hepatoduodenal Ligament Dissection

The gastrohepatic ligament is opened close to the inferior border of the liver taking care so as not to injure an accessory or replaced left hepatic artery arising from the left gastric artery. A large lymph node lying over the CHA (station 8a) is dissected and removed exposing the CHA clearly. It is then followed distally to expose the HA and GDA. A good length of GDA is cleared and it often requires ligation of supraduodenal branch that arises on to its right. As a routine we always clamp the GDA before ligation with a bulldog clamp to ensure good blood flow in the HA ruling out CA stenosis/obstruction (Fig. 6.3a). Next the GDA is divided between silk ties. Many surgeons would prefer to transfix the GDA stump with Prolene. GDA stump erosion and blowout is one of the causes of postpancreatectomy hemorrhage following a pancreatic leak/fistula, and hence GDA must be securely ligated. Right gastric artery and vein are also ligated (Fig. 6.3b).

The adventitial tissue over the porta hepatis is incised and all fat and fascia over the CHD/CBD are dissected down, thus taking away 12b1 and 12b2 lymph nodes. The CBD/CHD is dissected free and looped. The CBD/CHD is palpated to ensure no replaced or an accessory HA running posteriorly inadvertently missed on preoperative scans. Other major hepatic arterial anomalies are usually well identified preoperatively as is arterial involvement of GDA/HA and SMA wherein a cautious and different approach may be required. A sample of bile is collected for culture (Fig. 6.4a), cholecystectomy is performed (12c group of lymph nodes dissected en bloc), and CHD is transected. The proximal end of CHD is held in a bulldog clamp to prevent bile leakage, and the distal end is closed with silk sutures to minimize bile spill.

Following division of the CHD, the anterior wall of the PV is exposed, and all 12p group of lymph nodes are dissected down along. The fascia on the upper border of pancreatic neck is

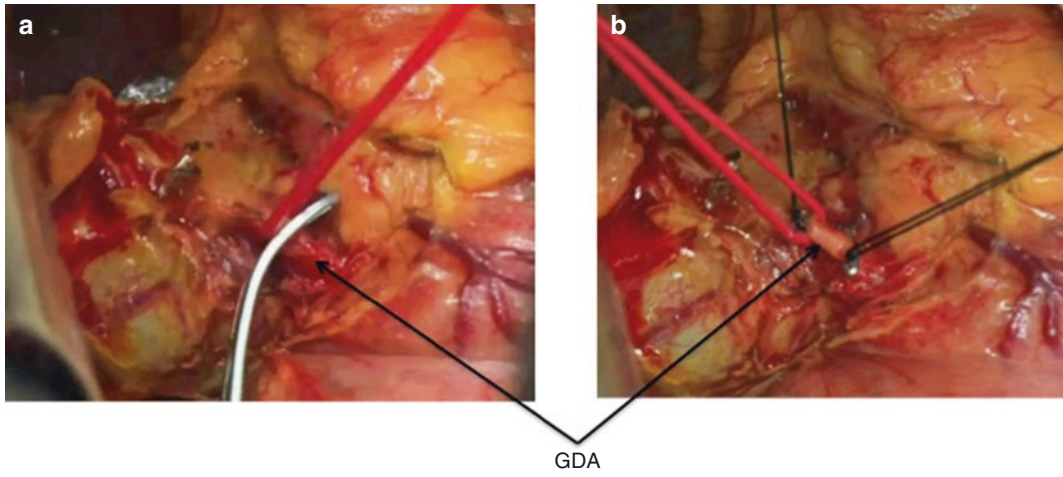

Fig. 6.3 (**a**) Gastroduodenal artery (GDA) is clamped with a bulldog and pulsations checked in the hepatic artery. (**b**) GDA divided after ligation

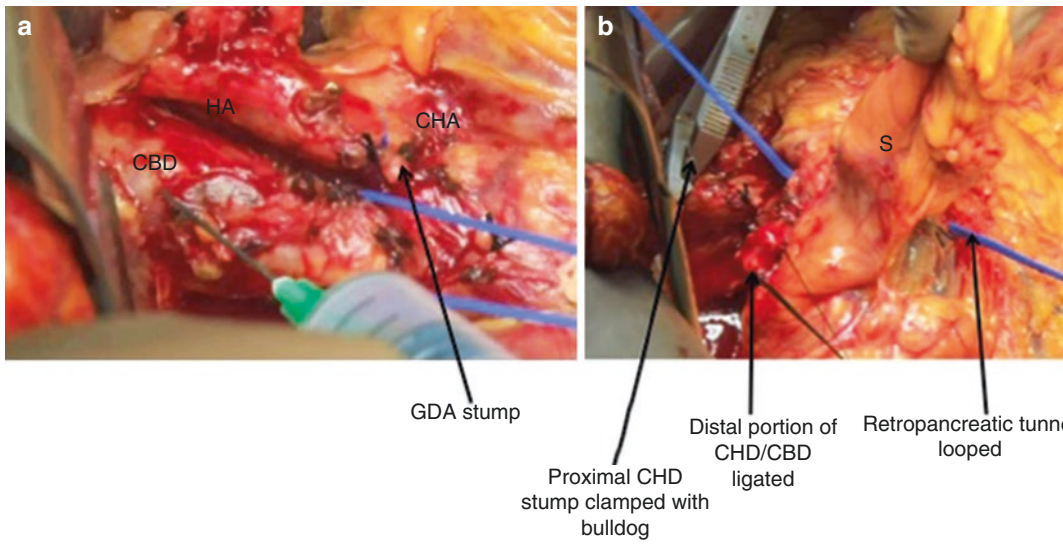

Fig. 6.4 (**a**) Common bile duct (CBD) is looped and sample of bile is collected for culture. HA, hepatic artery; CHA, common hepatic artery. (**b**) The common hepatic duct (CHD) proximally is clamped with a bulldog, and the distal end is ligated. The retropancreatic tunnel is completed, and an umbilical tape is passed through it. S, stomach

incised while retracting the CHD caudally and the GDA stump upward fully exposing the PV, thus meeting and completing the tunnel under the pancreatic neck already made during the first step of the operation. An umbilical tape is passed through this retropancreatic tunnel (Fig. 6.4b). Care is taken to protect the coronary vein (left gastric vein), if possible, as it terminates into the PV or at times at SMV-PV junction.

6.2.3 Extended Kocher Maneuver

The right hepatic flexure of the colon is mobilized inferiorly and the "C" of the duodenum is identified. IVC is exposed and the dissection continues starting behind the third portion of the duodenum sweeping all peripancreatic fat, fascia, and lymph nodes (station 13a, 13b) (Fig. 6.5a). The right gonadal vein is identified and protected.

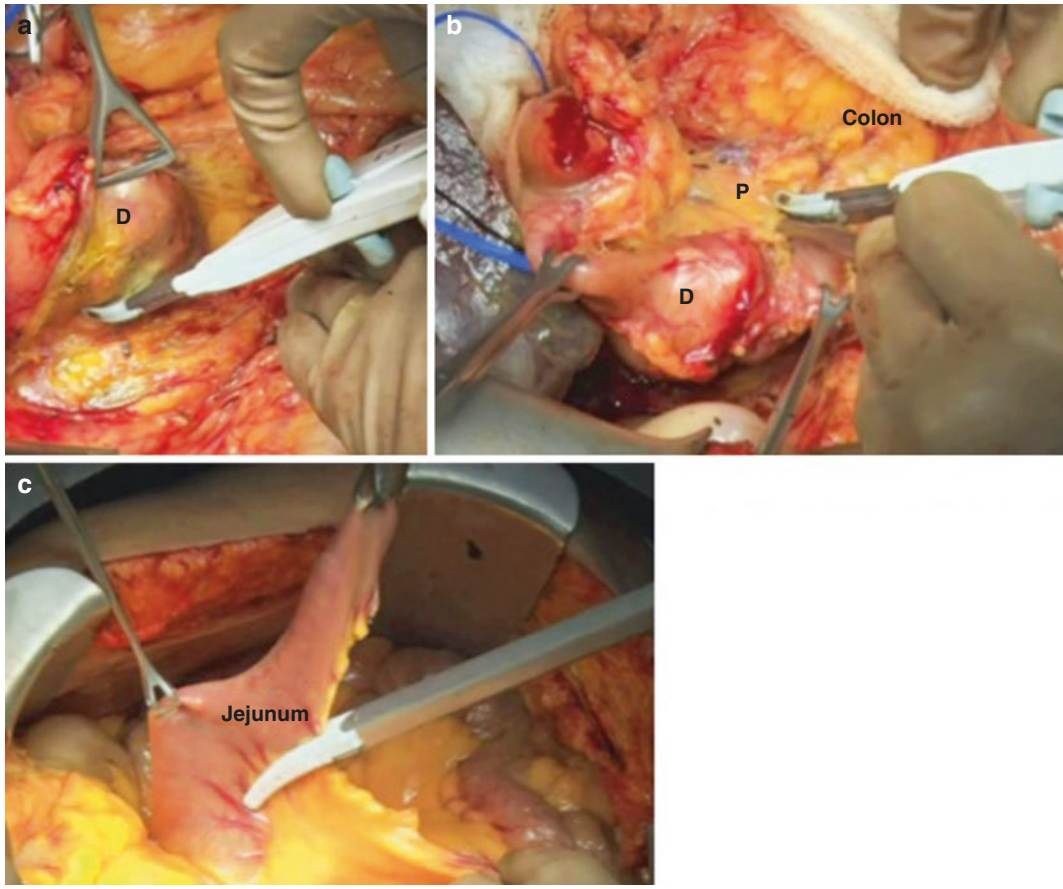

Fig. 6.5 (**a**) Extended Kocher maneuver is performed, *D* duodenum. (**b**) Anterior attachments of the transverse mesocolon to the pancreatic head (P) are taken down. (**c**) The jejunum and the duodenojejunal flexure are mobilized with a LigaSure device

Kocherization continues to the left of the aorta up to the DJ flexure exposing the left renal vein and the origin of SMA just above it. Any suspicious inter-aorto-caval lymph nodes are sent for frozen section. Anteriorly the attachment of the transverse mesocolon to the pancreas is taken down (Fig. 6.5b) along with all fat, fascia, and lymph nodes (station 17a, 17b) taking care not to injure the middle colic and the right colic vessels, and the SMV is exposed over the third part of the duodenum. Sometimes Cattell–Braasch maneuver is required wherein all the retroperitoneal attachments of the small bowel and right colon mesentery are mobilized up to the ligament of Treitz such as in patients with large uncinate tumor that may require venous resection and reconstruction.

6.2.4 Jejunal and Ligament of Treitz Transection

The transverse colon is lifted upward and the DJ flexure is exposed. The jejunum is transected with GIA linear cutter approximately 10 cm from the DJ flexure. The cut end of the jejunum is further mobilized by dividing its mesentery with a LigaSure device staying close to the jejunal wall (Fig. 6.5c). The loose attachments of the ligament of Treitz are taken down taking care to protect the inferior mesenteric vein (IMV) that lies just lateral to these attachments. The dissection continues from left to right mobilizing fourth and third part of the duodenum. The mobilized duodenum and jejunum are then reflected underneath the mesenteric vessels to the right upper abdomen.

6.2.5 Uncinate Dissection

We usually complete the uncinate dissection before proceeding with pancreatic neck and stomach/pylorus/duodenal transection, the irreversible step of PD. The transected jejunum is retracted laterally, and the SMV is gradually dissected free of the uncinate process by ligation/clipping of small venous tributaries draining in to the SMV. The first jejunal vein is identified and protected as it curves posteromedially from the right side of the SMV coursing posterior to SMA as it enters the medial aspect of the jejunal mesentery. Rarely the jejunal branch may be found anterior to the SMA. The uncinate process must be dissected off completely from the SMV to fully mobilize the SMV-PV confluence as well as to identify the SMA.

6.2.6 Division of the Stomach/Pylorus/Duodenum

Depending upon the tumor and the institutional policy, either the distal stomach or pylorus or first part of duodenum is transected. Thus, in a classical Whipple's (wherein antrectomy is performed by transecting the stomach at the level of the third or fourth transverse vein on the lesser curvature and at the confluence of the gastroepiploic veins on the greater curvature using a linear gastrointestinal stapler), in pylorus-resecting PD (PrPD) (wherein the stomach is divided just before the pylorus), and in pylorus-preserving PD (PPPD) (wherein the first part of the duodenum is divided 2–2.5 cm away from the pylorus), the lymph node stations 5 and 6 are removed en bloc with the specimen.

6.2.7 Pancreatic Neck Transection and Removal of the Specimen

The umbilical tape in the tunnel underneath the neck of the pancreas is lifted up to expose the PV. Four stay sutures in a figure-of-eight are taken on either side of the transection line at the superior and inferior borders of the pancreatic neck (Fig. 6.6a). These stay sutures not only stabilize the pancreas but also control bleeding from the blood vessels that run horizontally along the pancreatic borders during transection and in addition help during the pancreatico-enteric anastomosis in placement of sutures. Pancreas is next transected along the left border of the PV with either electrocautery or harmonic scalpel (Fig. 6.6b). Utmost caution is required if an electrocautery is used to transect the pancreatic neck. No metallic retractor or forceps should be in close contact with the pancreas and the PV underneath for there might be passage of current from the cautery to the PV underneath resulting in PV thermal injury and consequent hemorrhage. The pancreatic duct can be identified in most cases as it is cut. Some surgeons prefer to clamp and cut the pancreas with knife, but in our opinion it crushes the pancreas, causes bleeding, and hence may not be a good option.

The pancreatic head is retracted laterally while the PV is gently rotated medially facilitating dissection of the PV, SMV-PV junction, and SMV off the pancreas while ligating/clipping small venous tributaries carefully. One constant vein (some refer to it as posterosuperior pancreaticoduodenal vein) is always seen at the upper border of the pancreatic head behind the CBD. It should be neatly dissected and ligated/clipped as it could lead to significant hemorrhage if accidentally avulsed. Tumor involvement of SMV/SMV-PV junction/first jejunal branch can be resected en bloc with the specimen, and the technique is discussed in subsequent chapters. It is the last step of the operation wherein the tumor is left attached to the vein to be resected en bloc.

Medial retraction of the SMV-PV confluence facilitates dissection of the soft tissues adjacent to the right lateral wall of the proximal 3–4 cm of SMA (Fig. 6.7a). It is important to elevate/retract the SMV/PV with vein retractors so as to completely expose the SMA. This is the most important step in the operation from an oncologic perspective (retroperitoneal/SMA margin). The enveloping autonomic neural sheath is excised as the plane of dissection is directly on the adventitia of the SMA (lymph node stations 14a and 14b along the right lateral side of the SMA are removed). Commonly one or two inferior pancre-

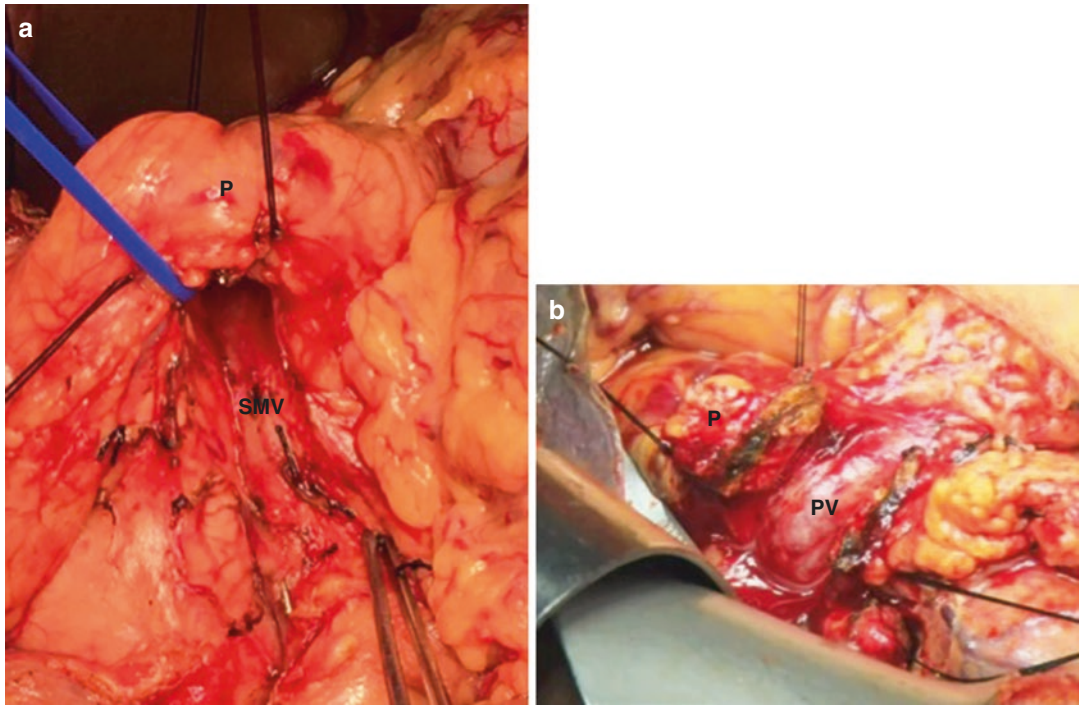

Fig. 6.6 (**a**) Four stay sutures are applied on the pancreatic neck (P). (**b**) The pancreatic neck is transected exposing the portal vein (PV)

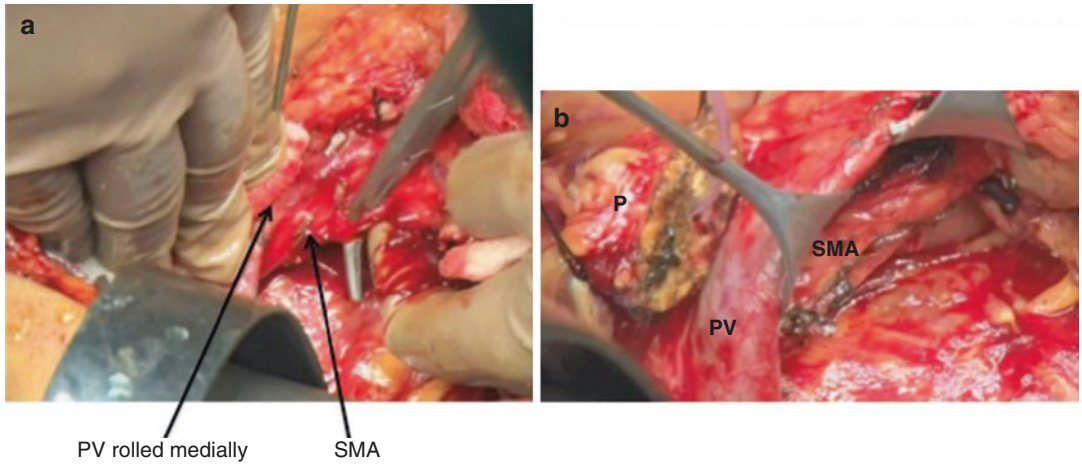

Fig. 6.7 (**a**) Dissection of the pancreatic head of the superior mesenteric artery (SMA) with the portal vein (PV) gently rolled medially. (**b**) The surgical field after the resection and removal of the specimen. P, pancreatic remnant; SMA, superior mesenteric artery; PV, portal vein

aticoduodenal arteries (IPDAs) can be identified and are ligated/clipped at their origin from the SMA (Fig. 6.7a). This dissection can be safely performed with the help of harmonic scalpel/LigaSure/bipolar cautery. The use of Endo GIA Stapler for this part of the operation [8] is discouraged as there remains a possibility of leaving behind some tissue and hence of a R1 resection that is best avoided. This completes the resection with fully cleared SMV/PV and the right half of the SMA (Fig. 6.7b).

Frozen sections of the pancreatic neck and CHD margins should ideally be sent and dissection tailored accordingly. The PD specimen must be oriented for the pathologist and the margins identified and inked/marked.

Conclusions

The above are the basic steps of performing PD, and several variations to the technique exist. Subsequent chapters in this book focus on variations in the technique of PD (PPPD, PrPD), PD with concomitant venous resections, and the importance of specimen orientation and margins from pathologic point of view.

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7 Pylorus-Preserving Pancreaticoduodenectomy for Pancreatic Cancer: How I Do It

Norbert Hüser, Volker Aßfalg, Matthias Maak, and Helmut Friess

Abbreviations

BDA	Biliodigestive anastomosis
IPMN	Intraductal papillary mucinous neoplasm
PDS	Polydioxanone suture
PJ	Pancreaticojejunostomy
PPPD	Pylorus-preserving pancreaticoduodenectomy
SMA	Superior mesenteric artery
SMV	Superior mesenteric vein

7.1 Pylorus-Preserving Pancreaticoduodenectomy: Are We Spoiled for Choice?

Pylorus-preserving pancreaticoduodenectomy (PPPD) is the standard resection procedure for pancreatic carcinoma besides the classical Kausch-Whipple operation whenever oncologically possible. Initially upcoming queries concerning oncological radicality and postoperative morbidity and mortality could be refuted by numerous randomized controlled trials [1]. Consequently this procedure increasingly gains acceptance not least because of the negative impact of partial gastrectomy on the development of jejunal ulcer and biliary reflux. The preference of either procedure belongs to the individual surgeon's expertise, and both are recommended for tumors of the pancreatic head [2].

The pancreatic anastomosis is usually performed by a mobilized jejunal loop. There are different techniques for reconstruction of the biliary drainage and intestinal passage like retromesenteric, antecolic, and retrocolic position of the loop. Dependent on the method used, either the whole loop is placed into the upper abdomen or the loop is cut and anastomosed [3].

The main focus of the entire operation is on the anastomosis of the pancreatic duct to the jejunal loop. One reason for the numerous techniques reported in literature is the serious consequence of any complication at the pancreatic anastomo-

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sis because of fistula, dehiscence, necrosis, or severe bleeding. Mainly two different anastomotic techniques are discussed: the so-called telescope anastomosis completely invaginates the pancreatic stump into the connected small bowel segment. This technique considers the hypothesis that fistulas generally start from the resection margin. However, the surgeon always has to bear in mind the risk that deep invagination of the pancreas may cause devascularization and ischemia because of too extended mobilization of the stump. Besides this technique, which is called *pancreatojejunostomy*, a distichous enlarged "duct-to-mucosa" anastomosis called *pancreaticojejunostomy* can be performed alternatively, as usually performed in our center. During this procedure the pancreatic duct is stitched directly to the jejunal mucosa and the slightly wider-opened intestinal wall, which is sutured to the pancreatic capsula and covers the stump's resection margin. However, no differences in regard to the occurrence of fistulas and general morbidity and mortality could be found [4]. Recently, the end-to-side anastomotic technique gains more and more attention besides the end-to-end anastomosis to meet the special requirements of an incongruity of the pancreatic resection margin and the jejunal lumen. In doing so, the anti-mesenteric cut of the priorly sealed jejunal loop can be much better adapted in regard to length and width to the cross-section of the pancreas.

A safe alternative to these techniques is the *pancreatogastrostomy* which does not show any differences in respect to fistulas, intra-abdominal colliquation, gastric emptying disorders, and overall morbidity and mortality, too [5, 6].

During the pancreatic anastomosis, there is the option for an intraluminal drainage to prevent the contact of alkaline pancreatic secretion with the anastomosis until wound healing is terminated. This drainage can either be performed by draining the jejunal loop (a drainage placed into the jejunal loop between biliodigestive anastomosis and pancreaticojejunostomy) or by a small silicone drainage (placed into the lumen of the pancreatic duct and tunneled through the jejunal wall). Numerous studies comparing these methods as well as the perioperative pancreatic duct stenting could not reveal any statistically significant advantages [7, 8] except for some specific conditions such as in the case of a small duct and soft pancreatic tissue [9]. Because of the potential risk of pancreatitis due to drainages and their uncertain effectivity and benefit, they are about to lose relevance [10, 11].

7.2 Pylorus-Preserving Pancreaticoduodenectomy: Surgical Procedure

Whenever interventional and conservative approaches failed to relieve of symptomatic duodenal, portal, pancreatic, or bile duct obstruction and especially in the case of (suspected) malignancy within the pancreatic head, partial pancreaticoduodenectomy is indicated. The most frequent diagnoses leading to this procedure are ductal pancreatic carcinoma, chronic pancreatitis, and papillary carcinoma. However, both malignant tumors like duodenal cancer or distal bile duct carcinoma and precursor lesions like intraductal papillary mucinous neoplasm (IPMN) may also require this surgical procedure. Of course, the necessity for an oncologically radical duodenopancreatectomy for IPMN has to be evaluated carefully in every single case. During the following explanations, we refer to the surgical steps in partial duodenopancreatectomy for pancreatic head cancer.

Hypothetically we present a patient with a suspicion for malignant lesion in the uncinate process of approximately 3.5 cm in diameter. An endo-ultrasound-guided biopsy was taken and confirmed the suspected malignancy in addition to an increased CA19-9 tumor marker serum concentration of 87 U/mL but normal CEA value. Anamnestically, the patient lost about 10 kg of body weight during the last 6 months, and the interdisciplinary tumor conference recommended surgical resection.

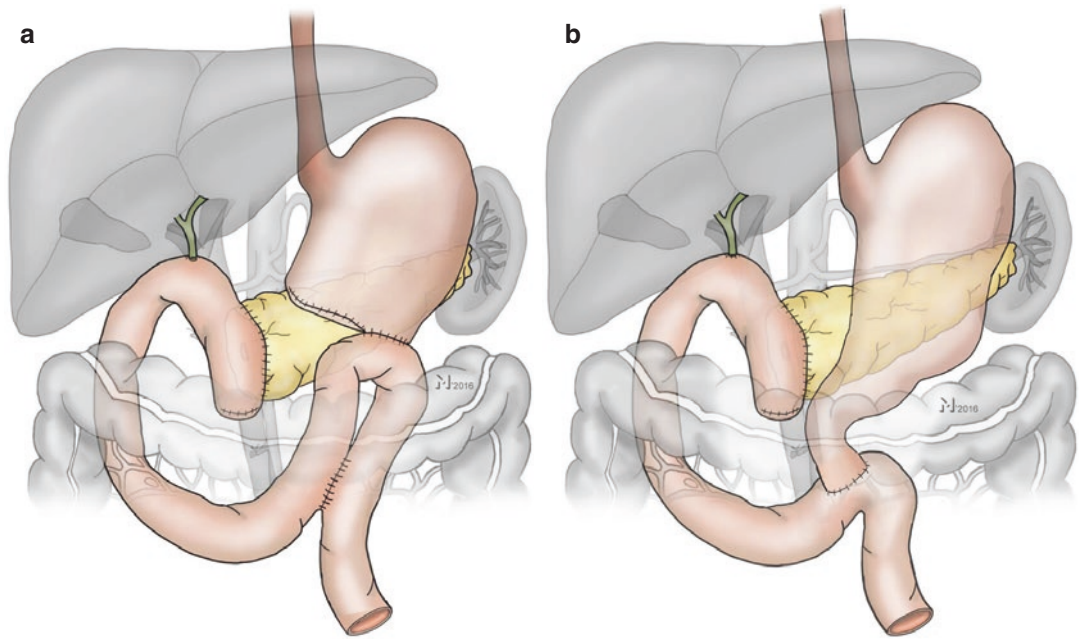

Fig. 7.1 Differences of classical Whipple procedure and pylorus-preserving Whipple. (**a**) The "classical Whipple procedure" is named after its describer and includes a total resection of the duodenum, the gallbladder and the common bile duct, the pancreatic head, and the distal third of the stomach. (**b**) The duodenopancreatectomy according to Traverso-Longmire recommends a post-pyloric duodenal cut. Both procedures require reconstruction by hepaticojejunostomy and pancreaticojejunostomy. The reconstruction may be performed by either one or more jejunal loops. However, we favor anastomoses to the first jejunal loop

In our center, we perform the pylorus-preserving pancreaticoduodenectomy (PPPD) according to Traverso and Longmire [12] and first described by Watson [13]. With this technique the stomach remains unaffected, and the duodenum is cut 2–3 cm distal of the pylorus. The required duodenojejunostomy for reconstruction of the intestinal passage is performed by an antecolic omega loop of the first jejunal loop. A Braun's foot-point anastomosis or a Roux-en-Y reconstruction is not necessary, respectively (Fig. 7.1). All patients are informed preoperatively regarding possible surgical extensions such as (partial) portal vein resection or total pancreatectomy for complete oncological tumor resection. It is a matter of course that patients are informed in detail about general risks (bleeding, thrombosis, embolism, an injury of organs, vessels, and nerves) and specific complications and risks of complex pancreatic surgery (anastomotic leakage or fistula of the biliodigestive anastomosis or the pancreaticojejunostomy, abscess, development of diabetes mellitus, exocrine pancreatic insufficiency, and arrosion bleeding).

The operative procedure can be divided into three major phases:

- Exploration and clarification of tumor resectability
- Resection
- Reconstruction

7.3 Exploration

The aim of the explorative phase is to give information on distant metastases, peritoneal carcinosis, and local resectability of the tumor, respectively. In the case of unresectable tumor spread, the strategy can be changed from the originally curative approach to a palliative procedure, e.g., a biliodigestive anastomosis or a double bypass operation with an additional gastroenterostomy [14, 15].

These are the surgical steps in detail:

- Team time-out, control of correct positioning of the patient, and application of a single-shot antibiosis approximately 15 min before skin incision.
- Skin disinfection and placing of surgical drapes.
- Longitudinal or transverse laparotomy of the upper abdomen by layer, correct dissection, opening of the abdomen and palpation of the liver, the whole small bowel, and the colon, and exclusion of peritoneal carcinosis.
- Application of a wound-edge protection device according to recent research results [16], an abdominal frame, and a retractor system (Fig. 7.2).
- Opening of the omental bursa after dissection of the gastrocolic omentum from the transverse colon and exposure of the ventral pancreatic surface. Dissection of the mesenterium of the transverse colon from both the pancreatic head and the duodenum (Fig. 7.3). This step allows for exclusion of an infiltration of both the stomach and the post-pyloric duode-

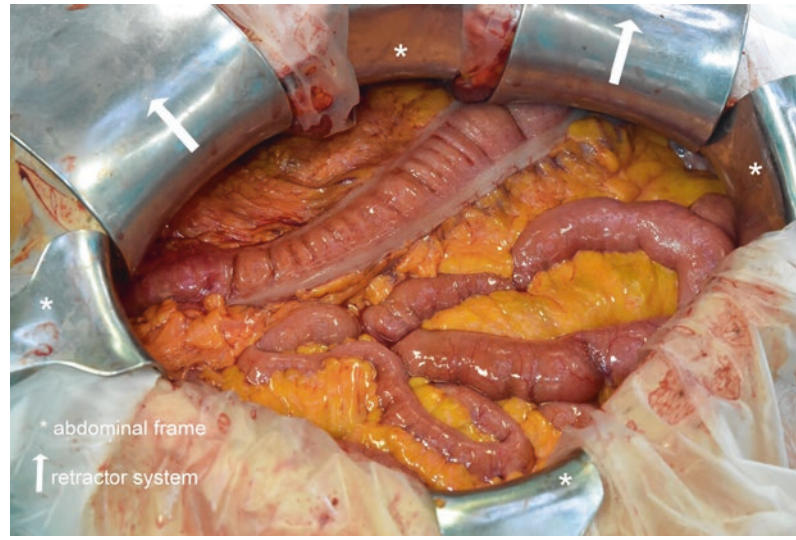

Fig. 7.2 Operating area with wound-edge protection, abdominal frame, and retractor system

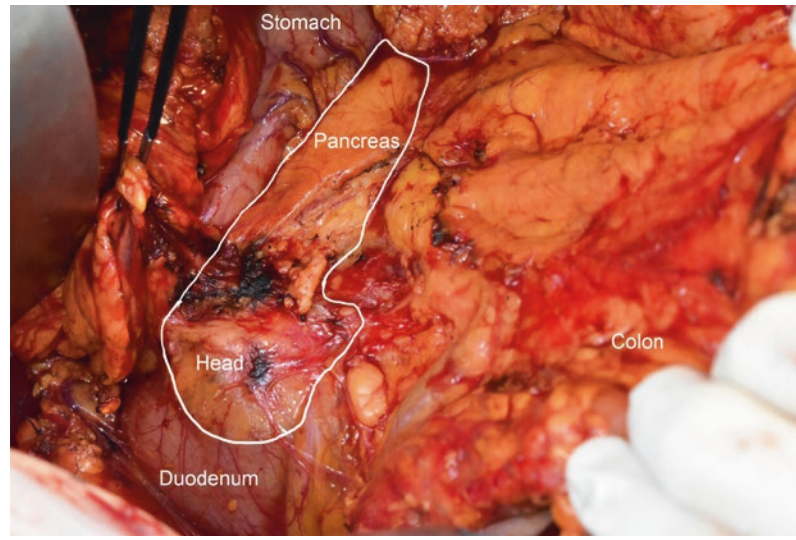

Fig. 7.3 Exposition of the pancreas after opening of the omental bursa

nal segment. Furthermore, the pancreas can now be easily explored to the left side. In case of an infiltration of the pyloric region, partial gastrectomy according to classical Whipple procedure should be considered.

- Performance of an extensive Kocher's maneuver for mobilization of the pancreatic head. Hereby exposition of the vena cava, the left renal vein, and the right ovarian/testicular vein which can be preserved. Extension of the mobilization of the duodenum and the pancreas towards the aorta and the entrance of the last duodenal part into the peritoneal cavity at the ligament of Treitz (Fig. 7.4).
- Bimanual palpation and examination of the pancreatic head from the omental bursa and the retroperitoneal space.
- Exposition of the superior mesenteric vein (SMV) at the inferior pancreatic margin (Fig. 7.5) and careful ligation with stitches (polybutester, e.g., Novafil 4/0) of both the anterior inferior and the posterior inferior pancreaticoduodenal veins.
- Blunt preparation and tunneling under the pancreas body straight on the SMV's plane

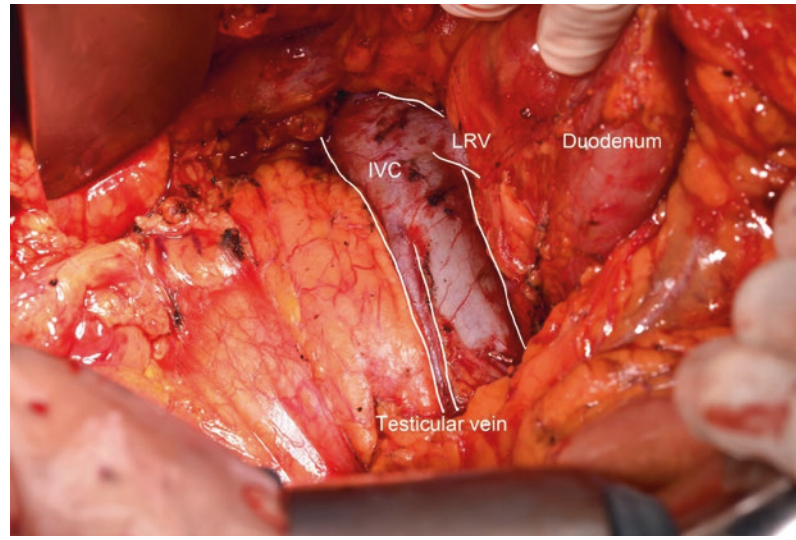

Fig. 7.4 Kocher's maneuver; IVC (inferior vena cava), LRV (left renal vein)

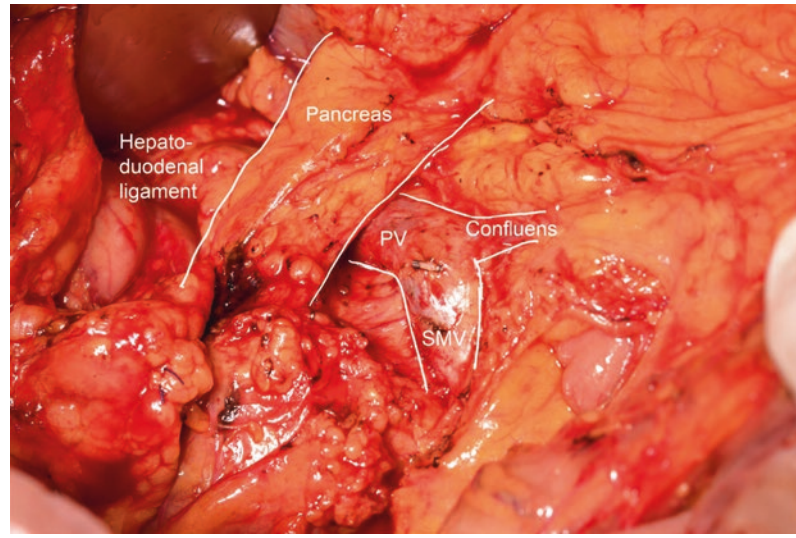

Fig. 7.5 Exposition of the SMV (superior mesenteric vein), venous confluence, and the PV (portal vein) at the inferior pancreatic margin

upwards to the venous confluence and application of support threads (polybutester, e.g., Novafil 5/0 or 4/0) at the inferior pancreatic margin. Evaluation of the resectability at the SMV and the superior mesenteric artery (SMA), which is also dissected carefully.

- Dissection and separate labeling of the structures in the hepatoduodenal ligament, which is usually started at the hilum of the liver and continued towards the pancreatic head. Careful identification of the anatomical course of the hepatic artery and identification of the branches towards the right and the left lobe (Fig. 7.6) with special attention to a potentially aberrant vascular supply. Dissection of the right gastric artery and investigative clamping of the gastroduodenal artery to verify the preserved arterial blood flow of the liver. Dissection of the common bile duct and finally labeling of the right and left hepatic artery, portal vein, and the common bile duct.
- Change towards the upper pancreatic margin and dissection of the local lymph nodes next to the hepatic artery straight down towards the coeliac trunk. Preparation of the portal vein and tunneling of the pancreas from the upper margin to conjoin both preparation planes. A silicone tube is placed under the pancreas to enable soft lifting, and support threads (polybutester, e.g., Novafil 4/0) are placed at the superior pancreatic margin, too (Fig. 7.7).
- Final evaluation of the resectability of the tumor when the pancreas can be tunneled completely in the portal vein's plane and arterial infiltration can be excluded.

7.4 Resection

In case of resectability, the duodenum, the gallbladder, and the pancreatic head are resected next.

- Dissection of the distal stomach and post-pyloric duodenum. Clip closure of the right gastroepiploic artery and vein at the prepyloric level and the right gastric artery by use of clips or an ultrasonic dissection device.
- Cutting of the post-pyloric duodenum with a linear stapler (Fig. 7.8) and wrapping of the closed stomach into a humid abdominal bandage before it is placed into the left upper abdomen for better overview.
- Cholecystectomy: antegrade dissection of the gallbladder, identification of both the cystic duct and the cystic artery, and closure with 3/0 Prolene sutures.
- Sectioning of the bile duct above the junction with the cystic duct with the scissor (to avoid

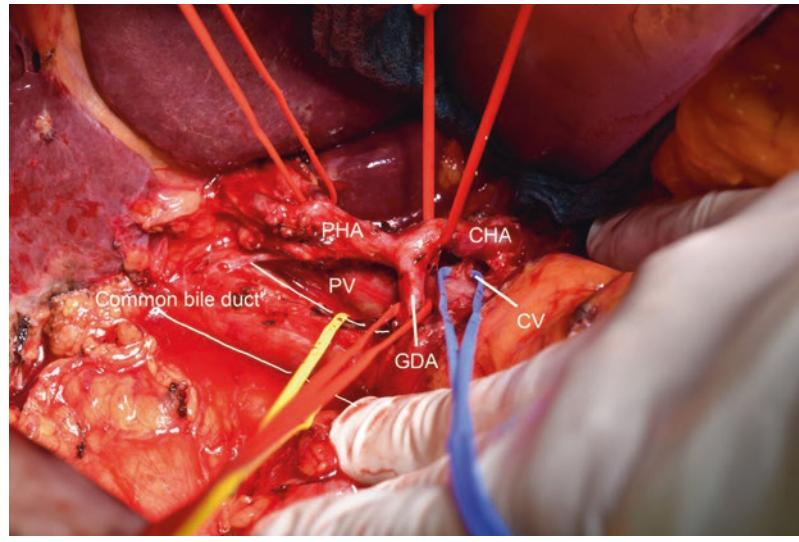

Fig. 7.6 Identification and labeling of the structures in the hepatoduodenal ligament; CHA (common hepatic artery), PHA (proper hepatic artery), PV (portal vein), GDA (gastroduodenal artery), CV (coronary vein)

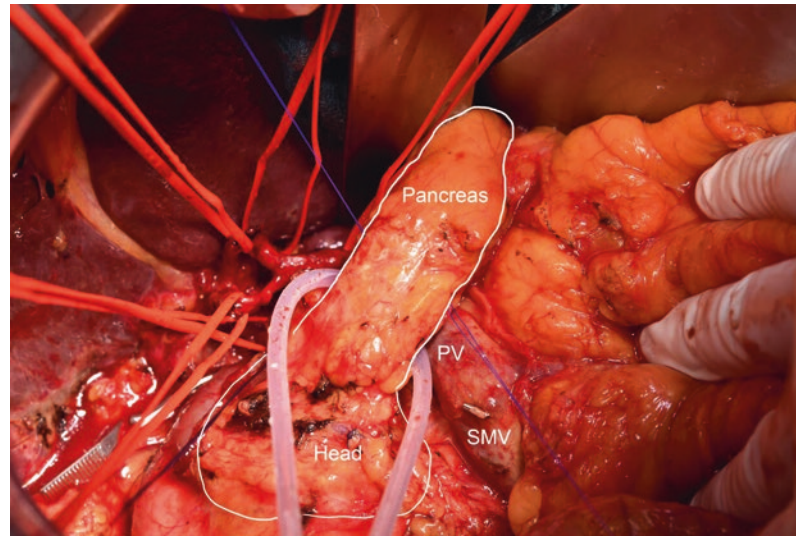

Fig. 7.7 Tethers at the mobilized pancreas; SMV (superior mesenteric vein), PV (portal vein)

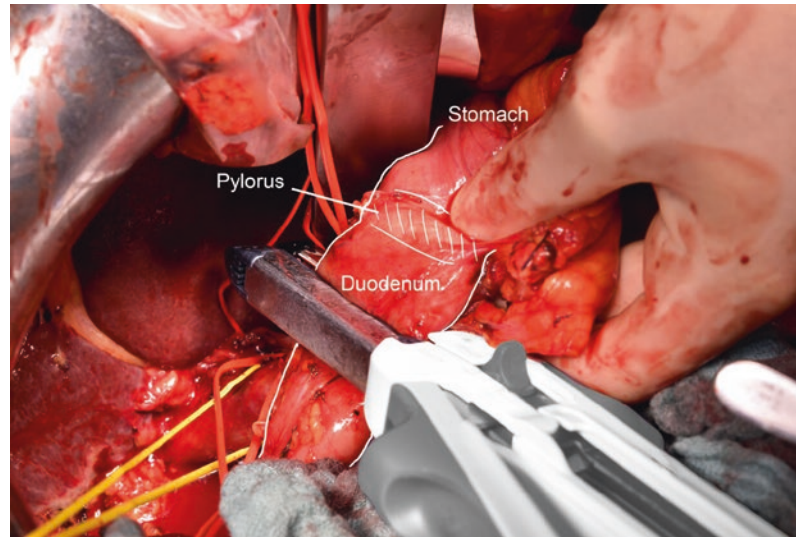

Fig. 7.8 Stapler cutting of the post-pyloric duodenum

thermic damage), acquisition of a microbiological swab, and flushing of the duct towards the intrahepatic distribution. Transient closure of the cut duct with a bulldog clamp. Further preparation of the duct towards the duodenum and intraoperative frozen section investigation of a bile duct resection margin specimen. Bleeding from the bile duct can be stopped by use of 5/0 PDS stitches.

- Continuation of dissection of the hepatoduodenal ligament after resection of the small omentum.
- Finishing lymph node dissection from the liver to the duodenum by use of bipolar pincette or ultrasonic dissection device and continuation of the dissection towards the celiac trunk including exposition of the left gastric artery and the splenic artery (Fig. 7.9).
- Sectioning of the gastroduodenal artery with three clips after investigative clamping (see exploration) to exclude an unexpected arterial blood supply of the liver via the superior mesenteric artery (Fig. 7.10).
- Dissection of the first jejunal loop after the ligament of Treitz has been dissolved and identification of the supplying mesenteric vessels by use of diaphanoscopy. Preparation

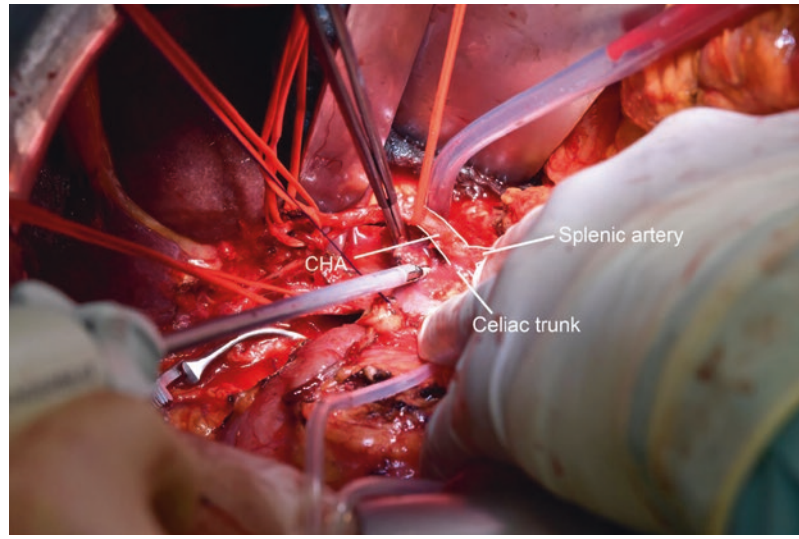

Fig. 7.9 Lymphadenectomy, exposition of the splenic artery and the celiac trunk; CHA (common hepatic artery)

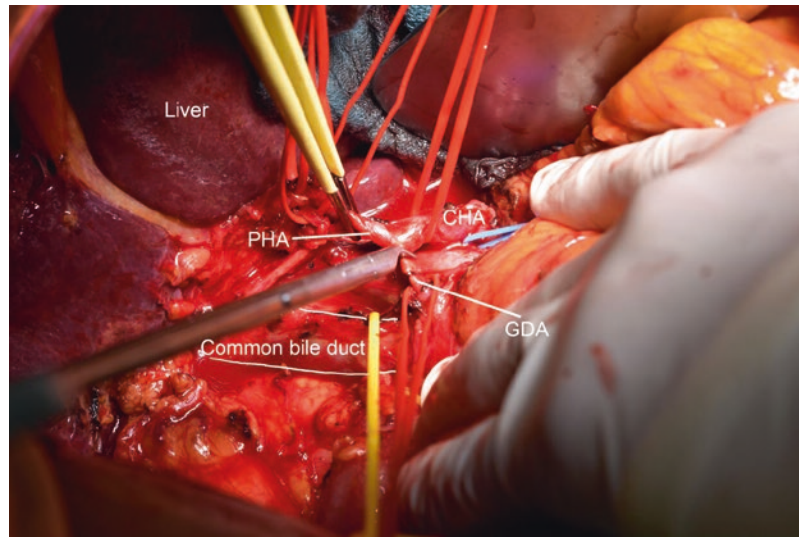

Fig. 7.10 Clipping with three clips and cutting of the GDA (gastroduodenal artery); CHA (common hepatic artery), PHA (proper hepatic artery)

of the vascular arcade with an ultrasonic dissection device and finally sectioning of the jejunum with the linear stapler-cutter device at an appropriate site.

- Tubular resection with an ultrasonic dissection device of the oral jejunal loop towards the former ligament of Treitz, sub-mesenteric pull-through of the mobilized jejunal loop to the right upper abdomen, and closure of the resulting hole with polybutester, e.g., Novafil 3/0 single stitches.
- Ligation of the pancreas towards the head and surgical sectioning of the pancreatic body over the portal vein (Fig. 7.11). Meticulous hemostasis with polybutester, e.g., Novafil 5/0 single sutures, at the left-sided resection margin and left dorsal mobilization of the pancreatic stump for approximately 2–3 cm.
- Inspection of the left resection margin and probing and flushing of the pancreatic duct with a buttoned cannula. Sending away of a frozen section for histopathologic investigation of the right resection margin.
- Radical completion of the resection of the pancreatic head and the uncinate process by use of an ultrasonic dissection device along the dorsal

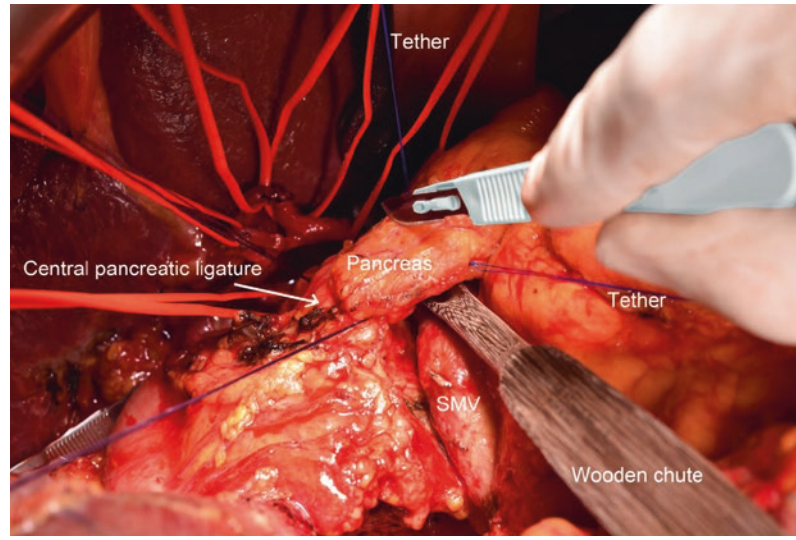

Fig. 7.11 Central pancreatic ligature and sectioning with the scalpel; SMV (superior mesenteric vein)

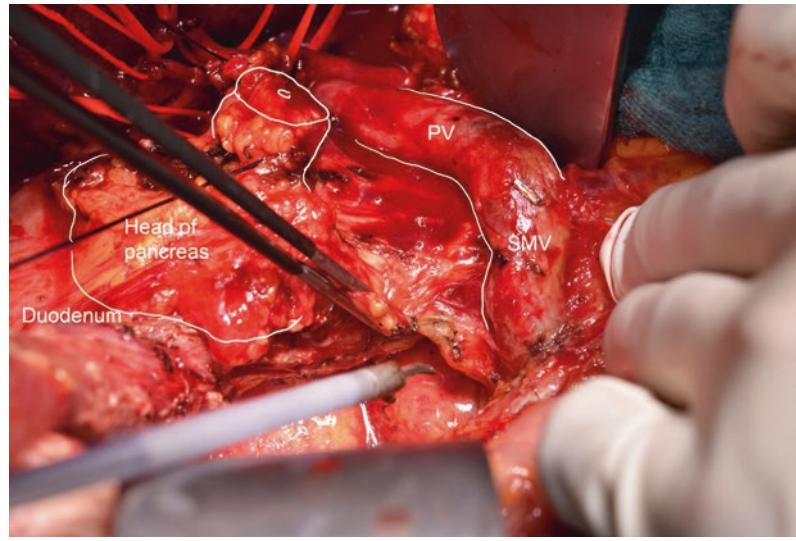

Fig. 7.12 Completion of the resection at the pancreatic head by use of a diathermia device and ligature of small vessels; PV (portal vein), SMV (superior mesenteric vein)

contact plane with the superior mesenteric artery and vein which ends on the left side of the vein (Fig. 7.12). Small vessels and the pancreaticoduodenal artery are dissected with a small Overholt and closed with clips or sutures. In case of infiltrative tumor spread into the portal vein or the superior mesenteric vein, the vessel segment can be resected en bloc together with the pancreatic head, and the blood flow can be rebuilt by direct end-to-end anastomosis with 5/0 Prolene or interposition of a vascular graft.

- Completion of the lymph node dissection around the superior mesenteric artery towards the celiac trunk. Careful inspection of the ventral and especially the dorsal resection plane at the retroperitoneal resection margin. Release of the histological specimen for pathological investigations.

7.5 Reconstruction

The reconstruction of the gastrointestinal passage is being performed during the reconstruction phase. For reconstruction of the gastrointestinal continuity, we perform the one-loop technique with a pancreaticojejunostomy (PJ) and a biliodigestive anastomosis (BDA).

In detail:

- Retrocolic elevation of the stapled jejunal loop after diaphanoscopy and creation of a passage through the transverse mesocolon on the right side of the middle colic artery.
- Tension-free placement of the jejunal loop at the pancreatic stump (Fig. 7.13) and additional inverting running suture over the stapler line for more safety.
- Suture of the *pancreaticojejunostomy in a two-layer technique* (Fig. 7.14a; the colors on both the jejunal loop and the pancreatic resection margin indicate the corresponding layers of the resulting anastomosis: I, dorsal outer layer; II, dorsal inner layer; III, ventral inner layer; IV, ventral outer layer): before the first row of stitches of the posterior wall is performed, we put three stitches at the front (Fig. 7.14b) and three stitches at the posterior wall (Fig. 7.14c) of the pancreatic duct, respectively. Dependent on the diameter of the pancreas, the exit of the 5/0 PDS stitches is placed within the parenchyma or even reaches the resection margin. The direction of the stitches at the posterior wall of the duct is *inside-out* and at the front wall is *outside-in*, respectively. It is important to leave the needle at the thread. The ends of the threads all have the same length and each of them is being marked with a small clamp. Next a humid abdominal bandage is placed around the retractor system, and the clamps of the front row are positioned on the bandage in a circle. To guarantee a maximum overview, a second humid bandage is placed on top, and the clamps of the posterior suture row are then placed on this bandage. In the next step, the first row of the posterior wall of the end-to-side anastomosis can be performed by 5/0 PDS *ventral-to-dorsal* stitches at the pancreas and seromuscular stitches at the jejunum (Fig. 7.14d). The number of single stitches depends on the diameter of the organ, and the distance between them is approximately 0.4 cm (direction of the stitches: pancreas, *inside-out*; jejunum, *outside-in*). In the next step, all threads of the posterior wall are tied. Now the jejunal lumen can be opened antimesenterically over a length of approximately 0.8–1 cm (Fig. 7.14e). Afterwards the stitches of the second posterior row are performed including the initially placed three posterior ductal stitches (Fig. 7.14f). For better overview these three stitches are completed first (direction of the stitches: jejunum, *outside-in*; *full-wall technique*). Afterwards the row of stitches can be finished to both sides. The stitches are separated by clamps, and then the clamps are stringed on a large Overholt clamp before the second posterior row is tied (Fig. 7.14g). It has to be noticed that the resulting incongruence of the opening of the jejunum on the one side and the smaller pancreatic duct on the other side needs to be closed by a

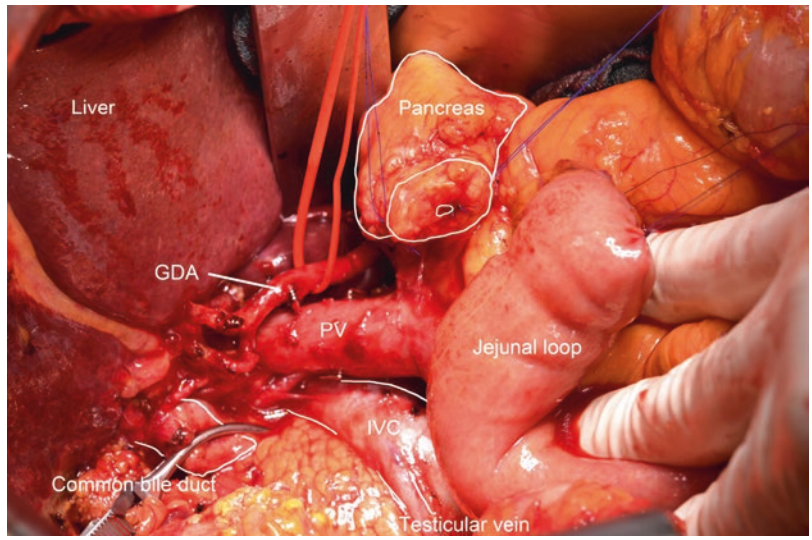

Fig. 7.13 Retrocolic tunneling of the jejunal loop and positioning for anastomoses; GDA (gastroduodenal artery), PV (portal vein), IVC (inferior vena cava)

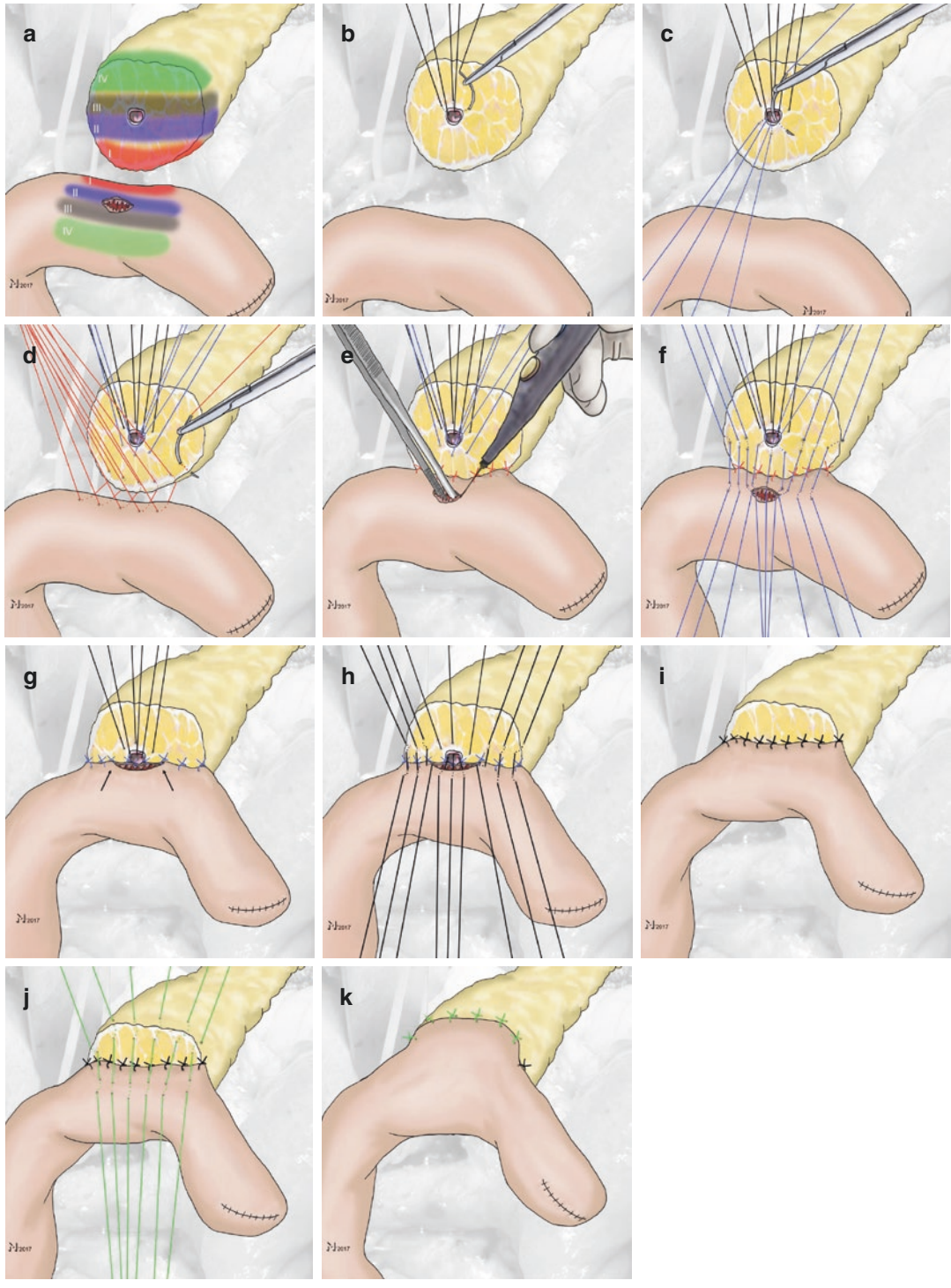

Fig. 7.14 Pancreaticojejunostomy (*detailed procedure see main body*)

single stitch between the pancreatic parenchyma (outside the duct) and the jejunal opening at each end of the duct-to-mucosa anastomosis (Fig. 7.14g arrow). The laterally extended lancing of the jejunal wall as compared to the diameter of the pancreatic duct ensures the direct flow of the aggressive pancreatic secretions into the bowel without resistance due to narrowing due to the sutures. After this step the first ventral row can be performed (Fig. 7.14h). The previously placed ductal sutures have to be completed at the jejunal side (direction of the stitches: jejunum, *inside-out*). Importantly, the stitches are placed again, separated with clamps, stringed by use of a large Overholt clamp, and finally tied like described before for the dorsal inner anastomotic row (Fig. 7.14i). In the last step, the second ventral row now can be performed placing stitches between the pancreatic parenchyma/capsule and the jejunal seromuscular wall (Fig. 7.14j) until the pancreatic resection margin is completely covered by the bowel serosa (direction of the stitches: pancreas, *outside-in*; seromuscular jejunum, *inside-out*) (Fig. 7.14k).

- *Biliodigestive Anastomosis (BDA)*: Approximately 8–10 cm distal of the pancreatic anastomosis, the BDA is being performed with 5/0 or 6/0 PDS single-stitch sutures (depending on the diameter and the consistency of the common bile duct's wall) after flushing the bile duct with sodium chloride 0.9%. Therefore an anti-mesenteric jejunal incision (length depends on the diameter of the bile duct) is necessary. The bile duct is usually stretched with two PDS 5/0 threads and a small clamp each at its left and right corners (Fig. 7.15a). First the two sutures at the corners of the BDA are placed (direction of the stitches: jejunum, *inside-out*; bile duct, *outside-in*; Fig. 7.15b). The two tethers can now be removed. Next, the ventral row with four to five threads is put at the jejunum (transmural; direction of the stitches: jejunum, *outside-in*; Fig. 7.15c). Importantly, the needle remains at the thread, and both ends of each thread are pooled with a small clamp and stringed with an Overholt clamp as described above. In the next step, four to five stitches can be performed to adjust the dorsal jejunal wall and the dorsal wall of the bile duct (Fig. 7.15d). The central stitch is put first and the row is then completed to both sides (direction of the stitches: jejunum, *inside-out*; transmural; bile duct *outside-in*). Dependent on the size of the bile duct, additional stitches are necessary for maximum tightness. The needles can be removed after every stitch, and the two ends of each thread are, respectively, pooled with small clamps and stringed with a large Overholt clamp. When all stitches are placed, the bowel can be moved carefully towards the bile duct. During this maneuver the tension of all threads has to be controlled carefully. Now the threads of the posterior wall can be sutured, the knots are automatically placed to the inner surface, and the threads are cut except for the two corner stitches (Fig. 7.15e). Afterwards the ventral wall of the BDA can be closed by using the previously placed stitches at the jejunum (direction of the stitches: bile duct, *inside-out*; Fig. 7.15f). Note that the threads of the two corner stitches are pulled towards the opposite side, while we perform the lateral stitches of the ventral wall to ensure an invaginating effect and safe closure of the posterior suture row (Fig. 7.15f arrow). However, after this maneuver the two threads are finally cut. The knots of the ventral part of the anastomosis are placed on the outside of the BDA (Fig. 7.15g).
- Finally, we place a white compress close to the BDA to identify potential anastomotic leakage by extravasating bile.
- The antecolic side-to-side *duodenojejunostomy* is performed with two continuous rows of PDS sutures at approximately 40 cm distal of the biliodigestive anastomosis. The stapler row at the duodenum is fixed with an Allis clamp, and the anastomosis starts with the posterior, seromuscular suture of the post-pyloric duodenum to the jejunum in end-to-side technique. Next, we perform an anti-mesenteric incision of the jejunum, which has exactly the same length as the duodenal width after resection of the GIA stapler line by use of the electric scalpel. Now the posterior wall is fixed with another Allis clamp for better overview, too. To prevent postoperative gastric emptying disorders, we insert a strong clamp into the pylorus and spread it gently. During the following step, the inner, transmural, continu-

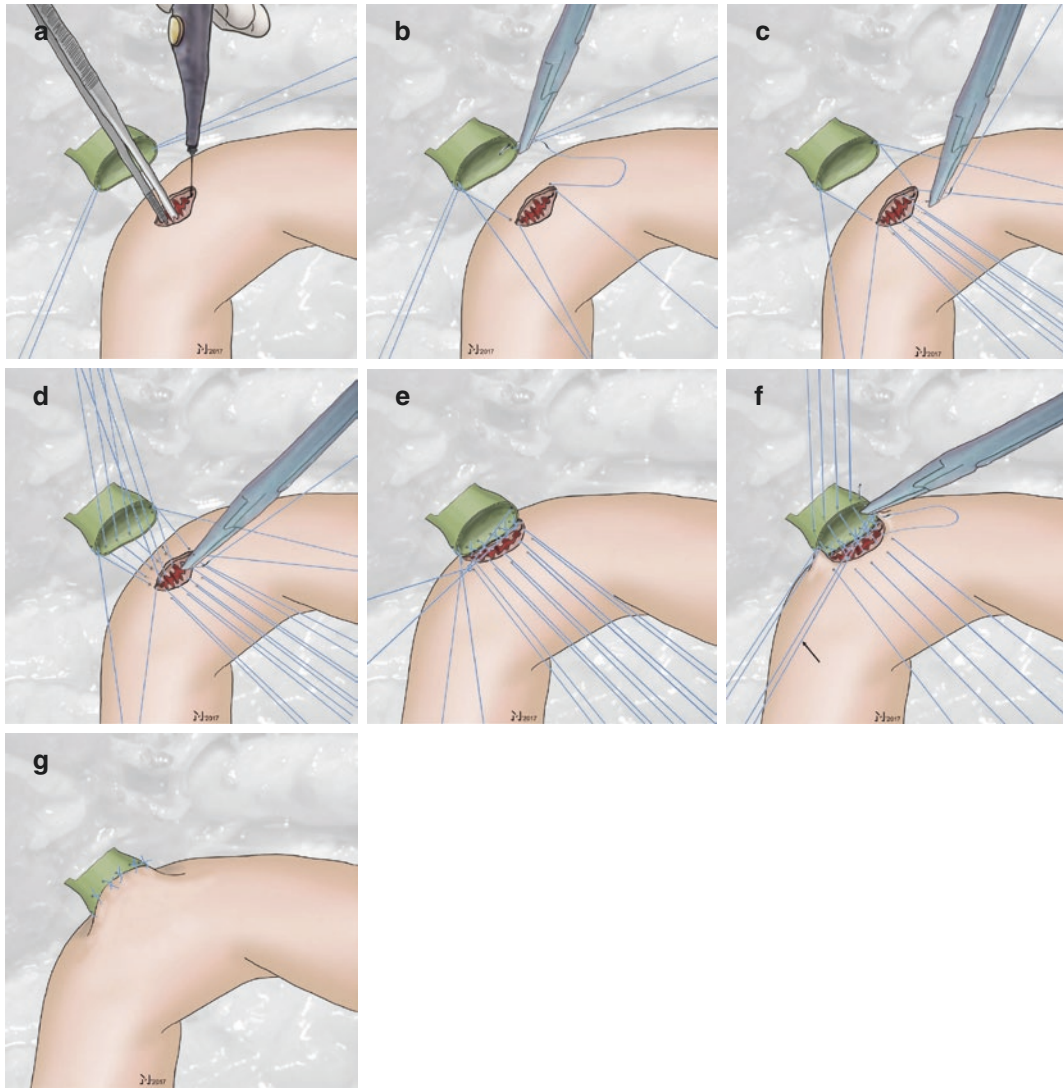

Fig. 7.15 Biliodigestive anastomosis (*detailed procedure see main body*)

ous posterior suture is completed and proceeds as far as one-third of the ventral wall before the intraluminal knot is made. Afterwards the inverted, transmural suture of the ventral wall starts in the corner and is completed at the just-mentioned knot. Finally, the continuous suture of the second (external) row (seromuscular–seromuscular) of the ventral wall is the last step of this anastomosis (Fig. 7.16).

- The mesenteric slit in the transverse mesocolon tunneled by the jejunal loop is then closed by several 5/0 PDS single-interrupted stitches to avoid obstruction of the jejunal loop.
- The whole procedure ends after all surgical cloths and gauze compresses are removed, the abdomen is flushed with warm saline, and in general two easy-flow drainages are placed at the pancreatic anastomosis and the bile duct anastomosis, respectively.
- The abdomen is closed by use of four continuous CTX sutures (two for the posterior and two for the anterior rectus fascia) and skin closure by a skin stapler.

Usually, the patient is monitored on the post-anesthesia care unit for 12–24 h.

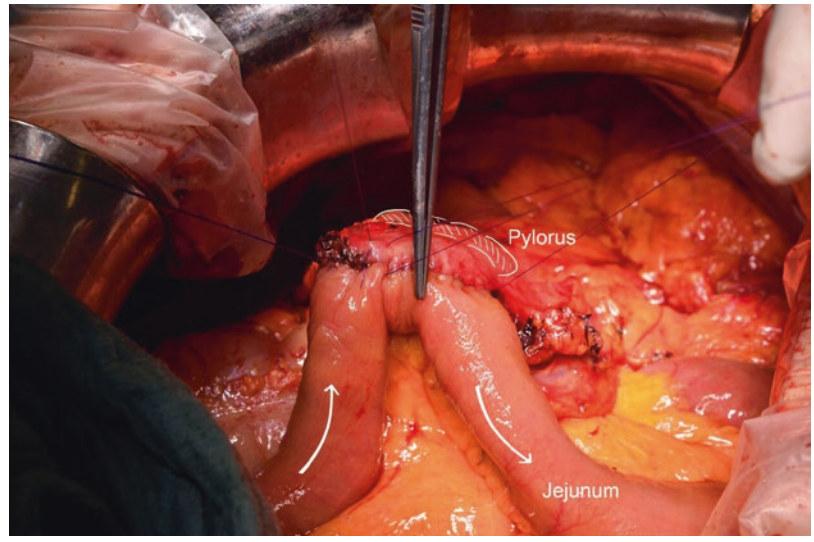

Fig. 7.16
Duodenojejunostomy

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8 Pylorus-Resecting Pancreaticoduodenectomy: How I Do It

Manabu Kawai and Hiroki Yamaue

8.1 Introduction

Pancreaticoduodenectomy (PD) has evolved since Kausch performed the first successful procedure as a two-stage operation in Germany in 1912 [1] and later developed by Dr. Allen Oldfather Whipple, the American surgeon, for the treatment of carcinoma of the ampulla of Vater in 1941[2]. Afterward, pylorus-preserving pancreaticoduodenectomy (PpPD), in which the whole stomach and 2.5 cm of duodenum were preserved, was described by Watson in 1944 [3] in an effort to decrease postgastrectomy syndromes in post-Whipple patients. Moreover, PpPD was popularized for the treatment of chronic pancreatitis as a modification of conventional PD reported by the American surgeons, Traverso and Longmire, in the late 1970s [4].

PpPD has been reported to reduce postgastrectomy syndromes such as dumping, diarrhea, and bile reflux gastritis or to have a better nutritional status than PD [5–9]. Therefore, PpPD has been generally accepted for surgical procedure of periampullary neoplasms such as pancreatic head cancer, cancer of ampulla of Vater, and bile duct cancer. Delayed gastric emptying (DGE) after PpPD is a frustrating and persistent complication. Moreover, it results in a prolonged hospital stay that induces to increase hospital costs and to decrease quality of life. To preserve pylorus ring with denervation or devascularization in PpPD may cause DGE. In 2007, subtotal stomach-preserving pancreaticoduodenectomy (SSPPD), in which duodenum and the stomach 2–3 cm proximal to the pylorus ring were removed, has been reported for periampullary and pancreatic head tumors of malignancy by the Japanese surgeon Hayashibe [10]. However, the definition of SSPPD in resection site of stomach remains unclear. It has reported in 2011 that the new surgical procedure resecting just pylorus ring in pancreaticoduodenectomy was designed as pylorus-resecting pancreaticoduodenectomy (PrPD) [11]. We will focus on the technical aspects and perioperative impacts of PrPD.

8.2 Procedure of PrPD

The following shows procedure of PrPD for pancreatic cancer. Mesenteric approach is performed for pancreatic cancer located in the pancreatic head.

8.2.1 Mesenteric Approach

- Mesenteric approach is an efficient and safe approach to pancreaticoduodenectomy when SMA involvement is suspected and makes it easy to determine resectability at the beginning of the operation.

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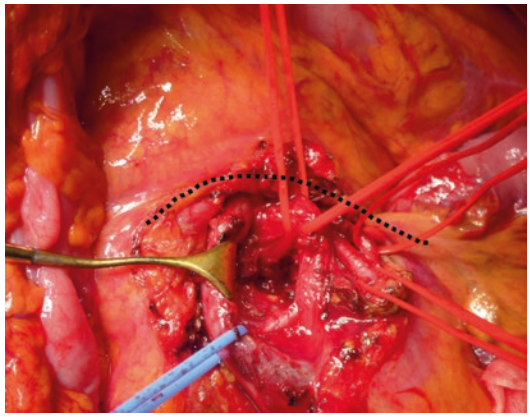

Fig. 8.1 Identification of SMA and SMV at the line between the Treitz ligament and the third portion of the duodenum (dotted line)

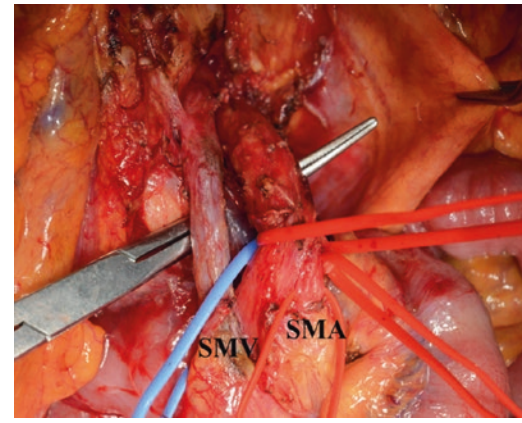

Fig. 8.2 The complete dissection of connective tissues of SMA and SMV via the mesenteric approach

- Early ligation of IPDA minimizes bleeding by better exposure and dissection of the posterior connective tissues of SMA-SMV.
- Useful approach in PV invasion with difficulty tunneling above PV.

First, the mesentery of the jejunum is resected at the line between the Treitz ligament and the third portion of the duodenum in order to identify the SMV and SMA at the line. SMV and SMA should be obtained using vessel loops. As the next step, the J1 and J2 branch are approached by exposing SMA (Fig. 8.1), and the inferior pancreaticoduodenal artery (IPDA) is also identified. After that, IPDA can be more readily ligated and divided. The connective tissues around the SMA and SMV are dissected completely (Fig. 8.2). If tumor is not invaded to the nerve plexus of the SMA, just lymph node dissection around the SMA is done. In this case, nerve plexus of SMA is preserved. In cases with abutment to SMA, the nerve plexus of the SMA should be resected in addition to this procedure in order to obtain negative surgical margins. The connective tissues along the SMV and SMA are dissected along its longitudinal axis toward the inferior border of the pancreatic body. On the way, the gastrocolic trunk root is ligated and divided. And then, tunneling is created between the anterior surface of the portal vein (PV) and the pancreas neck. In a case of invasion of the front side of the PV, tunneling between the anterior surface of the PV and the pancreas neck is impossible. However, in a case with invasion only of the right or left side of the PV, tunneling from the other side is possible.

8.2.2 Resection of Pylorus Ring

- The stomach is divided adjacent to the pylorus ring, and whole stomach is mostly preserved.

After mesenteric approach as artery-first approach, omentectomy is performed. The right gastric artery is dissected by the root, and the first pyloric branch is dissected around the pylorus ring. The first pyloric branch of the right gastroepiploic artery is also dissected along the greater curvature of the stomach. The pyloric branch of the vagal nerve is dissected along with lymph nodes around the pylorus ring (Fig. 8.1). In PrPD, the stomach is divided just adjacent the pylorus ring, and the nearly total stomach is preserved including antrum (Fig. 8.2).

8.2.3 Lymph Node Dissection Around Hepatoduodenal Ligament

- Precise identification and taping of the right hepatic artery to avoid injury of the right hepatic artery during exposure of the bile duct

Next, the adipose tissue around hepatoduodenal ligament is cleaned followed by the adipose tissue around the common hepatic artery. During this manipulation, gastroduodenal artery is identified, followed by common hepatic artery taping. Continuously, lymph node dissection around the proper hepatic artery from hepatoduodenal ligament is done while identifying portal vein front wall. Generally, the right hepatic artery runs behind bile duct. Therefore, it is important to identify the right hepatic artery to avoid injury of the right hepatic artery during exposure of the bile duct. After cholecystectomy, the bile duct is cut at the level of the common hepatic duct, and the margin of the bile duct is pathologically diagnosed to determine whether cancer cells are present. The bile duct margin of liver side is clamped with blood vessel forceps to prevent pollution of operative field by bile juice. After that, the origin of gastroduodenal artery is ligated and divided, and portal vein trunk is exposed.

8.2.4 Transection of the Pancreas

- The pancreas parenchyma is sharply transected with a cautery.

Before pancreatic resection, distal pancreas is gently fastened with a vessel loop to control bleeding from the remnant pancreatic stump. Caution must be used not to crush the pancreatic parenchyma during fastening by a vessel loop. The pancreas parenchyma is sharply transected with a cautery on the left side of the portal vein. Hemorrhage from the pancreatic stump of the remnant pancreas was ligated by 5-0 prolene. Preserving the blood stream of the surgical stump of the remnant pancreas is important to prevent pancreatic fistula. After complete hemostasis, 5-0 Fr pancreatic duct tube is inserted to confirm the patency and direction of the pancreatic duct.

8.2.5 Reconstruction

As the first step in reconstruction during PrPD, the proximal jejunum is brought through the transverse mesocolon by the retrocolic route. Duct-to-mucosa pancreaticojejunostomy during PrPD is done by a single layer of interrupted absorbable stitches. In seromuscular-parenchymal anastomosis, nonabsorbable interrupted stiches are placed in end to side. And then, a single layer choledochojejunostomy is constructed using interrupted stitches without a stent. Gastrojejunostomy in PrPD is performed by a two layer anastomosis via an antecolic route (Fig. 8.3). The final step is construction of the gastrojejunostomy using a two-layer anastomosis. The inner layer was 4–0 PDS-II and the outer layer used 3–0 silk for seromuscular anastomosis.

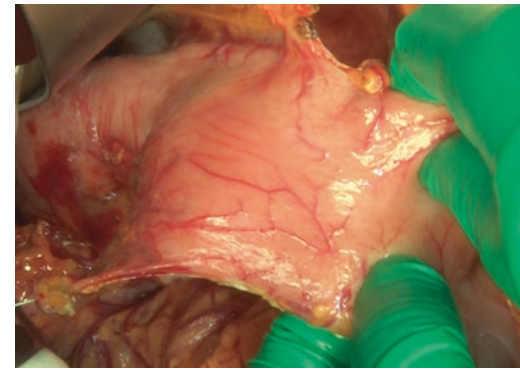

Fig. 8.3 Dissection around the pylorus ring; the right gastric artery is dissected by the root, and the first pyloric branch is dissected along the lesser curvature of the stomach. The first pyloric branch of the right gastroepiploic artery is also dissected along the greater curvature of the stomach

8.3 The Impact of Pylorus-Resecting Pancreaticoduodenectomy (PrPD)

DGE is a persistent complication after pancreaticoduodenectomy and results in significant prolongation of hospital stay. DGE after PpPD occurs due to several factors, such as (1) antroduodenal ischemia [12, 13], (2) gastric atony caused by vagotomy [14], (3) pylorospasm [15–17], (4) the absence of gastrointestinal hormones [18], (5) gastric dysrhythmia secondary to other complications such as a pancreatic fistula [19–21], and (6)

antroduodenal congestion [22]. In particular, DGE after PpPD has been attributed to denervation and devascularization of the pyloric ring due to pylorospasms caused by injuries of the vagus nerves innervating the pyloric ring. In PrPD, the only pylorus ring is resected. The stomach is divided adjacent to the pylorus ring, and almost whole stomach is preserved. PrPD was designed with expectation in maintaining the favorable stomach pooling ability and reducing the incidence of DGE compared to PpPD [11]. The technical modification of resecting pylorus ring may provide a simple and effective method to prevent the incidence of DGE (Fig. 8.4).

Table 8.1 shows summary for comparative study between PpPD and PrPD (SSPPD)

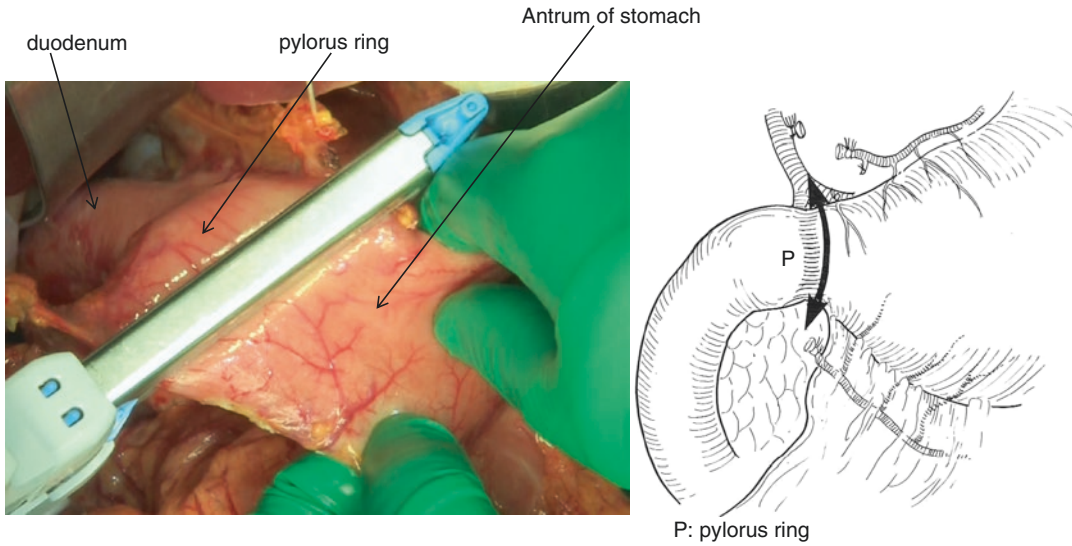

Fig. 8.4 Resection site of the stomach in PrPD; the stomach is divided just adjacent the pylorus ring

Table 8.1 Summary of comparative studies between PpPD and PrPD (SSPPD)

Authors	Study design	Years	Variable	Sample size	Definition of DGE[a]	DGE%	P value
Kurahara et al. [23]	Retrospective study	2010	PpPD	48	ISGPS[b]	34.8%	NS
			SSPPD	64		13.0%	
Kawai et al. [11]	Randomized controlled trial	2011	PpPD	64	ISGPS[b]	17.2%	0.024
			PrPD	66		4.5%	
Fujii et al. [24]	Retrospective study	2012	PpPD	33	ISGPS[b]	27.3%[c]	0.0012
			SSPPD	56		5.8%[c]	
Nanashima et al. [25]	Retrospective study	2013	PpPD	28	ISGPS[b]	46%[c]	<0.01
			SSPPD	27		7%[c]	
Hackert et al. [26]	Retrospective study	2013	PpPD	40	ISGPS[b]	42.5%	0.0066
			PrPD	40		15.0%	
Matsumoto et al. [27]	Randomized controlled trial	2014	PpPD	50	ISGPS[b]	20%	NS
			SSPPD	50		12%	

NS not significant, *PpPD* pylorus-preserving pancreaticoduodenectomy, *PrPD* pylorus-resecting pancreaticoduodenectomy, *SSPPD* subtotal stomach-preserving pancreaticoduodenectomy

[a]Delayed gastric emptying

[b]Pancreatic fistula is defined according to the International Study Group of Pancreatic Surgery (ISGPS)

[c]The rate of ISGPS grade B/C

[11, 23–27]. There are two RCTs and five retrospective studies which compared PpPD to PrPD (SSPPD) based on DGE defined by the International Study Group of Pancreatic Surgery (ISGPS) [28]. RCT which compared PpPD with PrPD demonstrated that PrPD (4.5%) resulted in a significant reduction in the incidence of DGE compared with PpPD (17.2%) ($P = 0.0244$) [11]. On the other hand, another RCT by Matsumoto et al. reported that the incidence of DGE was 20% with PpPD and 12% with SSPPD ($P = 0.414$) [27]. The RCT demonstrated that no significant difference in the incidence of DGE was observed between PpPD and SSPPD. Matsumoto et al. discussed that this discrepancy between two RCTS was due to differences in the study subjects. So, in their study, pancreatic cancer was excluded because patients with pancreatic cancer underwent a more invasive surgery including portal vein resection and regional lymph node dissection than other benign or low-grade malignant lesions. However, Fujii et al. reported that SSPPD offer better perioperative and long-term outcomes for pancreatic cancer compared PpPD [24]. Two meta-analysis comparing PrPD with PpPD reported that PrPD resulted in a significant reduction of the incidence of DGE compared to PpPD [29, 30]. As a modified anastomosis to prevent occurrence of DGE in SSPPD, Nakamura et al. demonstrated the greater curvature side-to-side anastomosis of gastrojejunostomy [31]. In the side-to-side anastomosis, the jejunal loop is anastomosed to the greater curvature 5–10 cm proximal to the closed gastric stump, and the anastomosis is just the greater curvature, not the anterior nor the posterior wall of the stomach. The study reported that the incidence of DGE in side-to-side anastomosis was in 2.5 % in side-to-side anastomosis and 21.3% in end-to-side anastomosis ($P = 0.0002$). It was concluded that the greater curvature side-to-side anastomosis of gastrojejunostomy significantly reduced incidence of DGE compared to the gastric stump-to-jejunal end-to-side anastomosis in SSPPD. Now, PROPP study which compares PrPD to PpPD by RCT with sample size for 89 patients per group has been proceeding by Hackert et al. in Germany [32] (Fig. 8.5).

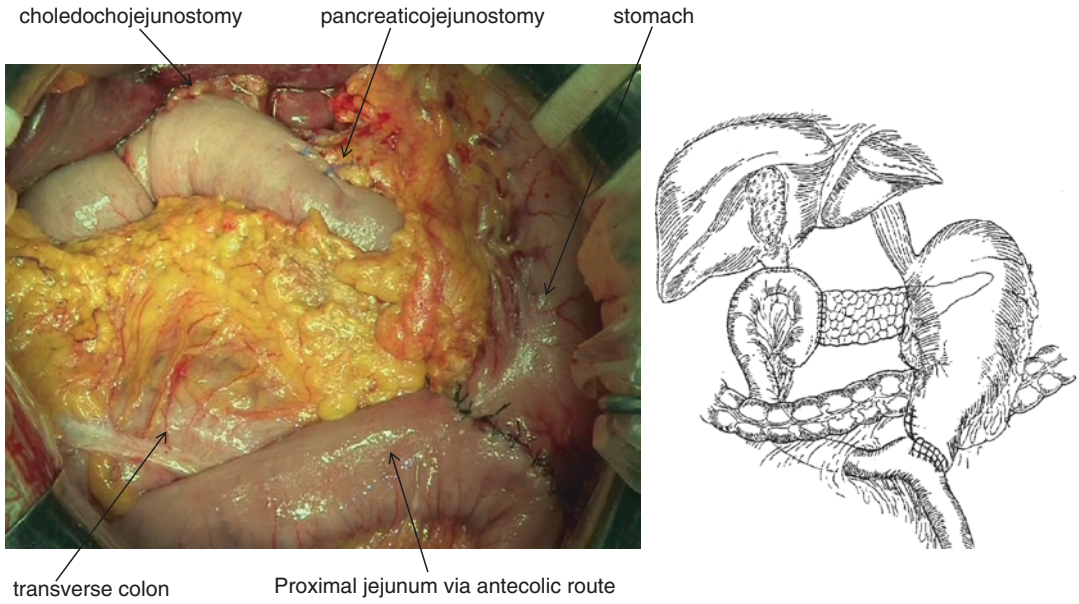

Fig. 8.5 Gastrojejunostomy in PrPD is performed by a two-layer anastomosis via an antecolic route

8.4 Long-Term Outcomes in PrPD

Advances in surgical techniques and perioperative management have led to a low mortality rate and long post-PD survival. Therefore, long-term outcomes after PD have been becoming a great matter of concern. In particular, nutritional status, body weight loss, dumping syndrome, or diarrhea after PD affects quality of life (QOL). The superiority of PrPD regarding long-term outcomes compared to PpPD remains still controversial. PrPD may have as an equally favorable pooling ability in the stomach as PpPD. However, PrPD with resection of the pylorus ring may result in the more frequent occurrence of dumping syndrome than PpPD. The study for 2-year follow-up period between PpPD and PrPD has shown that dumping syndrome occurred in only 1 of 66 patients (1.6%) with PrPD. The patients with dumping syndrome could be treated with dietary management alone. The study concluded that PrPD offer similar long-term outcomes with PpPD regarding QOL, nutritional status, and late complications [11]. The RCT by Matsumoto et al. also reported that SSPPD is equally effective in long-term nutritional status comparing to PpPD [27]. The study demonstrated that no significant differences were observed between PpPD and SSPPD regarding postoperative serum albumin levels, serum cholesterol levels, and body mass index during the 3-year follow-up period. On the other hand, Fujii et al. reported that serum albumin concentration and total lymphocyte count at 1 year postoperatively were significantly higher in SSPPD than in PpPD for patients with pancreatic cancer ($P = 0.0303$ and $P = 0.0203$, respectively) [24]. As the reason, they discussed that the gastric outlet diameter was larger after SSPPD than after PPPD, and this may have contributed to improved oral intake followed by more favorable nutritional status in their study.

Conclusion

PrPD is one of the procedures that may be recommended for treatment of periampullary neoplasms including pancreatic cancer. Two meta-analysis comparing PrPD with PpPD reported that PrPD resulted in a significant reduction of the incidence of DGE compared to PpPD. Further studies are required to clarify the long-term QOL and/or nutritional status resulting after the use of these techniques.

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9 Pancreaticojejunostomy: How I Do It

Andrew C. Gagel and Matthew H. G. Katz

The past three decades have witnessed a reduction in the rate of overall mortality associated with pancreatectomy to approximately 2% at high-volume pancreatic treatment centers. Nonetheless, as many as 75% of patients who undergo pancreatectomy suffer from at least one postoperative adverse event [1]. Among these, postoperative pancreatic fistula (POPF) remains the most feared. The impact of POPF may range from clinically insignificant to severe, leading to reoperation or death [2]. Indeed, total pancreatectomy was historically advocated for most patients with neoplasms in the head of the pancreas in large part to eliminate the possibility of POPF [3]. However, total pancreatectomy for adenocarcinoma is now performed only in the rarest of occasions, and pancreatoduodenectomy is favored. Management of the remnant pancreas is therefore compulsory.

Although simple ligation of the pancreatic duct was initially reported for this purpose, construction of a pancreaticoenteric anastomosis to either the jejunum or stomach is now a routine at pancreatoduodenectomy as it is associated with lower rates of POPF and exocrine dysfunction than duct ligation [4, 5]. A large number of surgical techniques have been devised to construct the pancreaticoenteric anastomosis—a testament that no single procedure is convincingly superior in this regard. I favor a variant of the two-layer Blumgart pancreaticojejunostomy characterized by (a) transpancreatic sutures that invaginate the pancreatic parenchyma into the jejunum and (b) a duct-to-mucosa anastomosis on the antimesenteric side of the bowel [6]. This technique differs from other techniques that utilize sutures tangentially placed through the capsule and are therefore subject to shear forces and are at high risk for disruption of the pancreatic parenchyma [7]. Indeed, the original technique described by Blumgart has shown to reduce leakage rates and surgical complications after pancreatoduodenectomy [8, 9]. The variant I use is simple and safe, and I have found that it can be taught relatively effortlessly to surgical trainees. And, it can be reproduced using minimally invasive approaches.

9.1 Pancreatoduodenectomy

At The University of Texas MD Anderson Cancer Center, we perform pancreatoduodenectomy using a standard technique. The six basic steps have changed little over the past two decades (Fig. 9.1) [10]:

1. The lesser sac is entered through the avascular plane between the omentum and transverse

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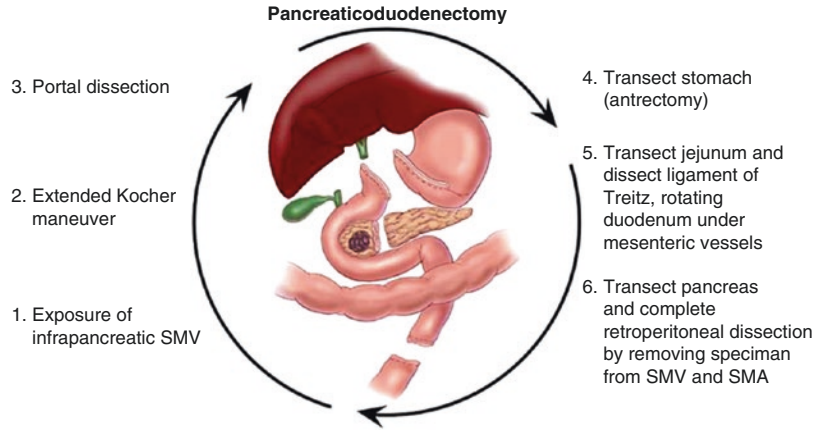

Fig. 9.1 Six steps of pancreatoduodenectomy as performed at the University of Texas MD Anderson Cancer Center

colon. The right colon is mobilized at the white line of Toldt until it has been completely medialized. The infrapancreatic superior mesenteric vein is identified by following the course of the middle colic vein to the root of the mesentery. The superior mesenteric vein is dissected free craniocaudally over the third portion of the duodenum.

2. A Kocher maneuver is performed to mobilize the duodenum and head of the pancreas to the level of the left renal vein.
3. A meticulous portal dissection is performed to expose the common hepatic artery both proximal and distal to the origin of the gastroduodenal artery. The gastroduodenal artery is then ligated and divided. The gallbladder is dissected from the liver, and the common hepatic duct is transected just cephalad to its junction with the cystic duct. The portal vein is exposed by dividing the common hepatic duct and performing cephalad retraction of the common hepatic artery. All lymphatic tissue is swept caudally.
4. If the pylorus is to be preserved, the duodenum is transected 1–2 cm distal to the pylorus to preserve a cuff for anastomosis. Otherwise, a standard antrectomy is performed.
5. The jejunum is transected approximately 10 cm distal to the ligament of Treitz. The jejunal and duodenal mesenteries are sequentially ligated and divided to the level of the aorta. The duodenum and jejunum are then rotated beneath the mesenteric vessels.
6. The pancreas is transected at the level of the portal vein. The specimen is separated from the superior mesenteric vein by ligating and dividing the small venous tributaries to the uncinate process and the pancreatic head. The superior mesenteric artery is completely exposed, and the lateral aspect of the vessel is skeletonized in the periadventitial plane to its origin at the aorta. This step is crucial for achieving a negative superior mesenteric artery margin, which is one of the main drivers of good oncologic outcome. The specimen is then removed from the abdomen.

Reconstruction is initiated in a similar, but reverse, stepwise fashion. Three anastomoses are constructed: (a) end-to-side pancreaticojejunostomy, (b) end-to-side hepaticojejunostomy, and (c) end-to-side duodenojejunostomy or gastrojejunostomy. The pancreaticojejunostomy, hepaticojejunostomy, and duodenojejunostomy/gastrojejunostomy are typically constructed sequentially along the jejunum, which is brought into the upper abdomen in a retrocolic position for this purpose. Occasionally, I use a Roux-en-Y reconstruction to isolate the duodenojejunostomy/gastrojejunostomy from the other anastomoses in the setting of a pancreas at high risk for POPF.

9.2 Technique of Pancreaticojejunostomy

The pancreaticojejunostomy is constructed in two layers. Organization of the sutures placed in the anastomosis may be facilitated by the use of suture retainers. In the absence of these devices, Kelly clamps fastened upright to the surgical drapes can be used to organize rubber-shodded hemostats attached to each suture. I typically fasten one Kelly clamp to the upper right and one to the upper left of the incision (Fig. 9.2).

The stapled jejunal limb is oversewn using Lembert sutures of 3-0 silk, and it is then brought into the upper abdomen through a rent in the transverse mesocolon. The limb is positioned adjacent to the pancreatic remnant, and the length of the pancreatic surface is mapped with a marking pen onto the limb of the jejunum to assist with suture placement. The anastomosis is then constructed in the following steps (Fig. 9.3):

1. Starting at the cephalad aspect of the anticipated anastomosis and working caudally, seromuscular sutures of pledgeted, double-armed, 4-0 prolene are placed in the jejunal limb. The needle is placed perpendicular to the long axis of the jejunum to create each mattress stitch; typically two or three sutures are placed cephalad and two or three caudad to the pancreatic duct. Care must be taken to avoid piercing the pancreatic duct with medial sutures, a pitfall that may be particularly likely in the setting of a large and "floppy" duct and atrophic gland. Once all of these sutures are placed in the jejunum, each is sequentially passed through and through the pancreas approximately 0.5–1 cm distal to its cut surface. They are then pulled taut so the jejunal limb and deep surface of the pancreas are well-approximated (Fig. 9.3 (1)).
2. The sutures on the pancreatic side of the anterior wall of the duct-to-mucosa layer are placed next, again starting cephalad and moving caudally. I use 5-0 prolene for this purpose; precise suture placement, particularly in the setting of a small duct, is facilitated by the use of double-armed sutures, so bites can be taken from the inside of the pancreatic duct outward toward its transected surface (Fig. 9.3 (2)). Once these sutures have been placed, they are "hung" on the suture retainer so that the duct is held wide open. The posterior layer of the duct-to-mucosa anastomosis can thus be fashioned with greater precision.
3. A small jejunotomy is created just opposite the pancreatic duct opening using electrocautery, and the posterior aspect of the duct-to-mucosa is then created (Fig. 9.3 (3)). Bites are initiated through the pancreatic duct and out the deep surface of the pancreas, then brought through the jejunal limb and out through the jejunotomy. Care must be taken to obtain a full-thickness bite of jejunum that includes mucosa. The orientation of the sutures should be carefully placed in a clock-face orientation like "spokes on a wheel" in such a way that they appear to radiate out from the epicenter of each orifice. The posterior sutures are then tied down in a manner that is simultaneously gentle and firm. The completed knots will lie inside the anastomosis (Fig. 9.3 (4)).
4. The hanging anterior sutures are then passed into the jejunotomy and out the surface of the jejunum, again "like spokes on a wheel", and sequentially tied down. The duct-to-mucosa anastomosis is now complete (Fig. 9.3 (4)).

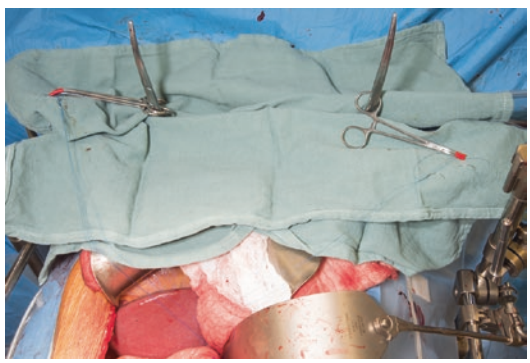

Fig. 9.2 Kelly clamps fastened upright to the surgical drapes are used to organize sutures during construction of the pancreaticojejunostomy (photograph)

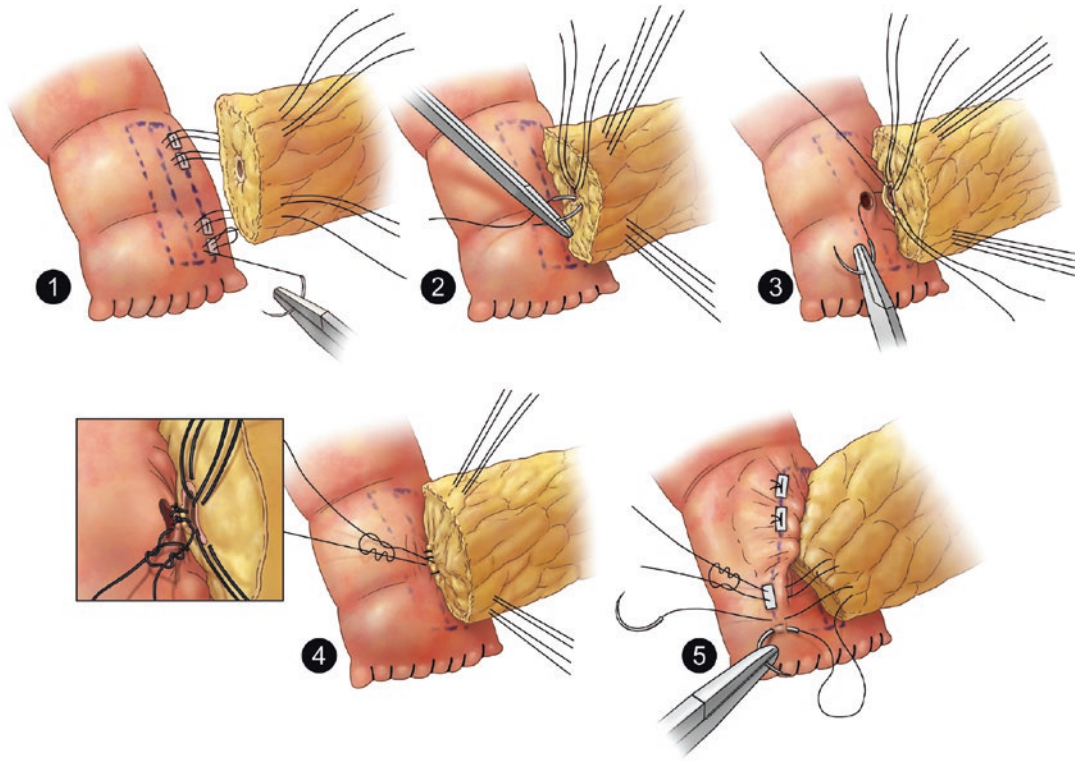

Fig. 9.3 Steps of pancreaticojejunostomy

5. Finally, the first double-arm suture is then used to make a mattress stitch on the anterior side of the jejunum, again with the needle placed perpendicular to the long axis of the bowel. The jejunum is then rolled over the pancreatic remnant, invaginating the pancreatic parenchyma and the duct-to-mucosa anastomosis. Each mattress suture is passed through a pledget and is then tied down (Fig. 9.3 (5)).
6. We place a single Jackson-Pratt drain to drain the pancreaticojejunostomy given randomized data that it is beneficial [11].

9.3 Perioperative Care

We utilize two distinct clinical pathways for the postoperative care of patients who undergo pancreatoduodenectomy based on their risk for POPF [12]. Preoperative clinical factors—histopathologic diagnosis, pancreatic duct diameter and body mass index—are used to estimate risk for clinically significant POPF as very low (~0%), low (~10%), high (~30%), or very high (~60%). Patients at very low or low risk for POPF are targeted for a hospital length of stay of 6 days or fewer and are accelerated through their hospitalization by removing the nasogastric tube on day 2 and removing the surgical drain on day 3. Pharmacologic prophylaxis against POPF is not utilized in this group of patients. In contrast, patients at high or very high risk for POPF are treated more conservatively. Their hospital length of stay is targeted for 10 days, and they receive pasireotide in the perioperative period in an attempt to reduce clinically significant POPF [13].

I favor this technique and use it irrespective of gland texture or duct diameter because successful management of the pancreatic remnant depends on the surgeon's concentration and on his/her familiarity and experience with technique [14]. However, as long as the basic tenets of a safe

anastomosis are met—careful handling of the tissues, tension-free adaptation, good perfusion, and an absence of distal obstruction—any pancreaticoenteric anastomotic technique can have a good outcome.

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10 Invaginating Pancreaticojejunostomy: How I Do It

Carrie D. Walsh, Charles J. Yeo, and Harish Lavu

10.1 Introduction

In the early years of pancreatic surgery, PD was associated with a high rate of mortality. However, with the effort of many surgeons working to improve the operative technique, in addition to advances in postoperative care, there has been a marked improvement in patient outcomes—with a typical perioperative mortality rate in high-volume centers of less than 2% [1].

Developments in the treatment of pancreatic disorders began as early as 1898, when Alessandro Codivilla, an Italian surgeon, performed the first partial resection of the pancreas, duodenum, stomach, and bile duct for treatment of carcinoma of the pancreas. Unfortunately, Codivilla's patient died from cachexia resulting from steatorrhea 18 days post-op [2]. It was not until 1912 when Walther Kausch, a German surgeon in Berlin, successfully performed a resection of the pancreas, in addition to a partial resection of the duodenum [3]. Like many surgeons operating at the beginning of the twentieth century, Kausch believed that the duodenum was vital for patient survival, and therefore his procedure did not include a complete duodenectomy. However, in 1918 Dragstedt et al. [4] disproved this misconception, demonstrating that dogs could survive following a duodenal resection, thereby setting the stage for Allen Oldfather Whipple to perform the first reported total duodenectomy in 1935 [5].

Building upon the findings of Kausch, Dragstedt, and others, Whipple and his resident John Hawk conducted a series of experiments on dogs, which allowed them to conclude that reimplantation rather than ligation of the pancreatic duct was an important step in reconstruction and could reduce the incidence of pancreatic fistula formation. Additionally, their experimental PJ showed that the connection between the epithelium of the pancreatic duct and the mucosa of the jejunum could heal within a 24-h period [1].

It was in 1935 that Whipple first published a report of three patients who underwent a two-stage procedure at Columbia-Presbyterian Hospital in New York [5]. The operation included the complete resection of the duodenum and a large portion of the pancreas. Unfortunately one of the patients died within 30 h of the procedure due to problems with anastomotic breakdown. The second and third survived for 9 and 24 months when they died of cholangitis and liver metastasis, respectively.

In 1946, Whipple published a second report, which addressed his 10-year experience in radical pancreatic and duodenal resection, and suggested changes to his original report [6]. This publication advocated for a one-stage procedure,

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following the discovery that vitamin K could correct the hypocoagulability associated with malabsorption of fat-soluble vitamins secondary to chronic biliary obstruction. It was in this second report that Whipple emphasized three central aspects of the operation: (1) the complete resection of the head of the pancreas and duodenum, (2) anastomosis of the pancreatic duct to a jejunal loop, and (3) a choledochoenterostomy in place of a cholecystoenterostomy. Aside from one significant variation that was described by Traverso and Longmire in 1978—the pylorus-preserving modification (PPPD) [7]—the current PD differs relatively little from the procedure described by Whipple in 1946.

The two most common PJ techniques currently in practice around the world are the invaginated and the duct-to-mucosa anastomoses. An advantage of the invaginated technique over the duct-to-mucosa is that the cut edges of the pancreas are invaginated or "dunked" into the jejunal lumen. This allows for the apposition of the pancreatic capsule to the jejunal serosa. Additionally, the technique can be applied even in a patient with a very small pancreatic duct [8] or a soft pancreatic texture [9]. However, despite its advantages, "dunking" requires the entire cut surface of the pancreas to be exposed to bile-activated pancreatic juice, which has the potential to lead to anastomotic breakdown [10]. The duct-to-mucosa technique does not require a large jejunotomy to facilitate pancreatic invagination. However, it can be difficult to perform in a patient with a small pancreatic duct and may leave the patient with an anastomosis that is prone to obstruction [10].

A number of prospective, randomized controlled trials have been conducted to attempt to compare the invaginated and duct-to-mucosa techniques (Table 10.1). The most recent study was performed by Xu et al. in Shanghai, China, in 2015 [10]. The primary variable under consideration was the occurrence of postoperative pancreatic fistula (POPF)—as defined by the International Study Group on Pancreatic Fistula (ISGPF). Although the Xu et al. study observed a slight superiority for the invaginated PJ technique, the authors emphasize that the risk of POPF remains multifactorial. The patient's BMI, the experience of the surgeon, operating time, and the texture of the pancreas are but some of the variables affecting patient outcomes. The most significant results favoring the invaginated technique were for patients with soft pancreas texture and a non-dilated main pancreatic duct, showing a POPF rate of 9.6% for the "dunking" technique in contrast to 27.3% for the duct-to-mucosa technique ($p = 0.001$) [10]. This finding is consistent with a dual-institutional prospective randomized controlled trial reported in 2009 by Berger et al. at Thomas Jefferson University and Indiana University, which showed a 12% POPF rate for the invaginated technique vs. a 24% rate ($p = 0.04$) for the duct-to-mucosa group [11]. A prospective randomized trial by Bassi et al. in 2003 showed no statistically significant differences between the two methods in patients with a soft pancreatic texture—with a 15% POPF rate for the invaginated approach and a 13% POPF rate for the duct-to-mucosa technique [13].

Despite these findings, the most important factors in anastomotic success are generally considered to be the proficiency and experience of the surgeon for the given technique that they favor.

10.2 Technique for Pancreaticoduodenectomy (PD): Resectional Phase [14, 15]

1. The operation is conducted with the patient in the supine position. Following abdominal exploration, a cholecystectomy is performed using the "dome down" technique, and the cystic duct and artery are ligated. The Kocher maneuver is then executed to release the duodenum from its retroperitoneal attachments and mobilize the pancreatic head, leaving the exposed tumor accessible for palpation. Dissection is then carried out within the gastrohepatic ligament. The common hepatic duct is encircled and transected. The gastroduodenal artery (GDA) is test clamped to ensure adequate proper hepatic artery flow before the vessel is controlled with 2-0 silk

Table 10.1 Prospective, randomized controlled trials comparing the invaginated PJ to the duct-to-mucosa technique

Author/year	Number of points	Incidence of POPF Grade (when provided)	
		Total: 14 (9%)	Total: 31 (20%)
Xu et al. (2015) [10] Study: October 2012–June 2014	*N* = 308		
	N = 155: invaginated (104 = soft/non-dilated duct 51 = hard/dilated duct)	Grade A: 13*	Grade A: 18*
	N = 153: duct-to-mucosa (95 = soft/non-dilated duct 58 = hard/dilated duct)	Grade B/C: 1*	Grade B/C: 13*
Berger et al. (2009) [11] Study: August 2006–May 2008	*N* = 197	Total: 12 (12%)	Total: 23 (24%)
	N = 100 (51%) invaginated	Grade A: 5 (5%)	Grade A: 6 (6%)
	N = 97 (49%) duct-to-mucosa	Grade B: 5 (5%)	Grade B: 14 (14%)
		Grade C: 2 (2%)	Grade C: 3 (3%)
#Langrehr et al. (2005) [12] Study: July 1999–December 2000	*N* = 113	2 (3.5%)	2 (3.6%)
	N = 57: invaginated/mattress suture technique		
	N = 56: duct-to-mucosa/Cattell anastomosis		
Bassi et al. (2003) [13] Study: 1999-2001	*N* = 144	11 (15%)	9 (13%)
	N = 72: invaginated		
	N = 72: duct-to-mucosa		

Key: *p <0.05; #underpowered study—no p-values provided

ties and a 3-0 silk suture ligature. The duodenum is transected 2–3 cm below the pylorus with a stapler. A Penrose drain is passed underneath the pancreatic neck overlying the superior mesenteric vein (SMV). This allows for safe transection of the pancreatic neck with electrocautery.

2. Using the base of the transverse mesocolon as an anatomic landmark, the ligament of Treitz is exposed and lysed. At a distance of 15–20 cm distal to the ligament, the jejunum is divided using a stapler, and the distal jejunal staple line is imbricated with 3-0 silk Lembert sutures. The proximal jejunum is then divided from its mesentery and moved to the right side of the surgical field by passing it under the base of the mesocolon and the superior mesenteric vessels. Working along the lateral border of the superior mesenteric artery (SMA) and SMV, the retroperitoneal margin of the uncinate process is dissected out, and all pancreatic tissue adjacent to the artery is separated from the perivascular plane. The specimen is removed and a hemostatic agent is applied to the retroperitoneal margin to promote clotting. A series of interrupted 3-0 silk sutures is used to close the defect previously created at the ligament of Treitz, with care taken not to injure the inferior mesenteric vein (IMV).

10.3 Technique for the Invaginated PJ [14, 15]

1. Just to the right of the middle colic vessels, a defect is introduced into the transverse mesocolon, and the proximal jejunum is carried through this defect.
2. The pancreatic remnant is mobilized for a distance of 2–3 cm from the underlying splenic vein (Fig. 10.1).

10.4 Posterior Outer Row of PJ [14, 15]

1. The PJ is constructed end-to-side, with an interrupted posterior outer row of 3-0 silk mattress sutures placed between the posterior aspect of the pancreatic remnant and the jejunum. In a patient with a characteristic "soft" pancreas, we find that the sutures hold best when placed in a horizontal mattress fashion (Fig. 10.2).

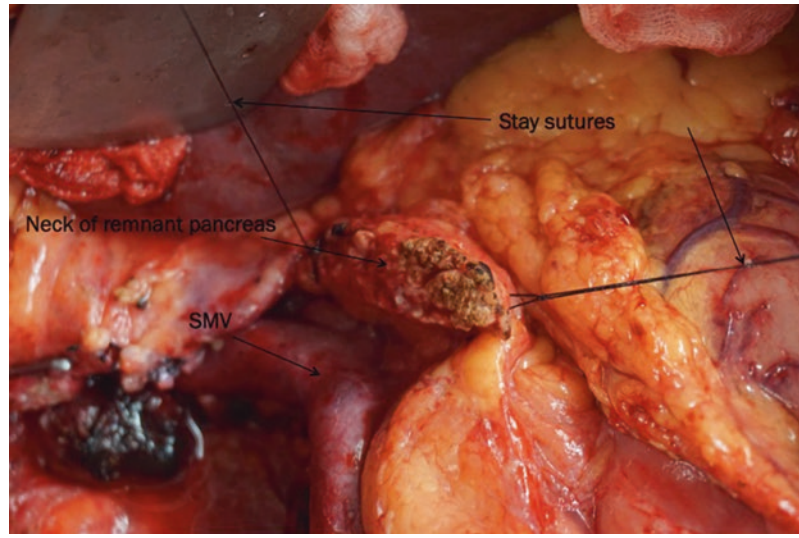

Fig. 10.1 The pancreatic remnant is mobilized for a distance of 2–3cm from the underlying splenic vein

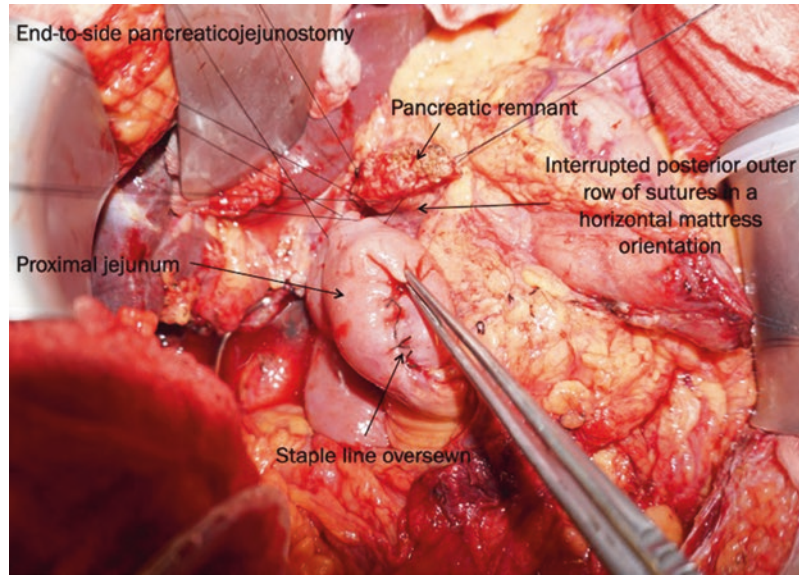

Fig. 10.2 The PJ is constructed end-to-side, with an interrupted posterior outer row of 3-0 silk sutures placed between the posterior aspect of the pancreatic remnant and the jejunum. In a patient with a characteristic "soft" pancreas, we find that the sutures hold best when placed in a horizontal mattress fashion

2. Once the sutures are secured and tied down (Fig. 10.3), electrocautery is used to perform the jejunotomy, and a vein retractor is used to expose the jejunal mucosa.
3. Care should be taken to ensure that the jejunotomy is shorter than the width of the cut surface of the pancreas, as the small bowel will stretch during construction of the anastomosis.

10.5 Inner Rows of PJ [14, 15]

1. A 5 French pediatric feeding tube is placed within the pancreatic duct to ensure that the duct is not inadvertently ligated during the construction of the anastomosis (Fig. 10.4). For larger pancreas ducts, an 8 French pediatric feeding tube can be used.

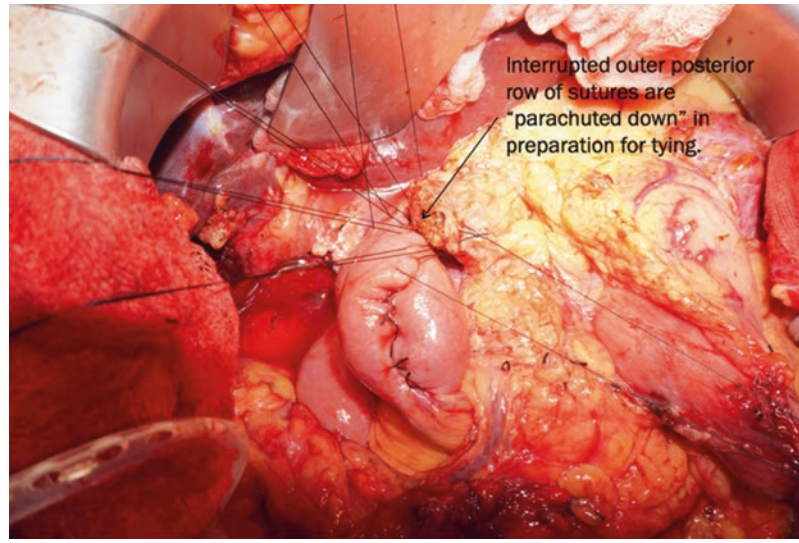

Fig. 10.3 Once the sutures are secured and tied down, electrocautery is used to perform the jejunotomy, and a vein retractor is used to expose the jejunal mucosa

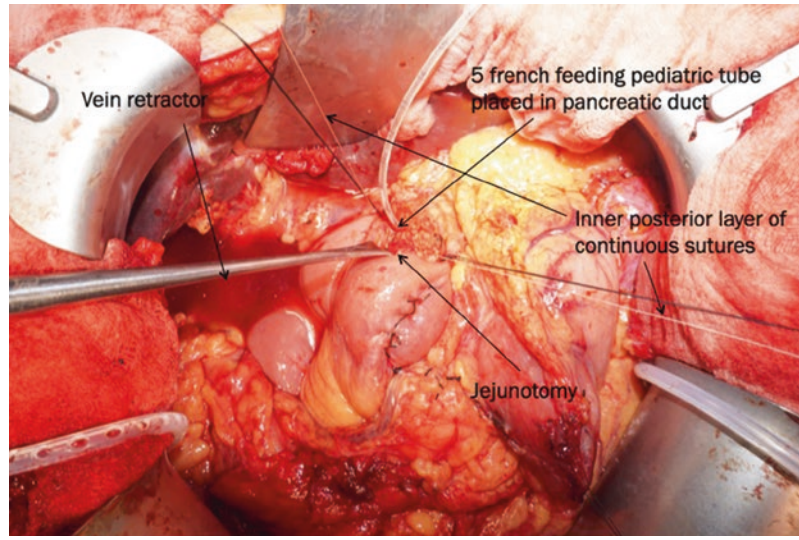

Fig. 10.4 A 5 French pediatric feeding tube is placed within the pancreatic duct to ensure that the duct is not inadvertently ligated during the construction of the anastomosis

2. Two 3-0 Polysorb™ sutures are then placed in a running-locking fashion in the inferior corner of the anastomosis. One stitch is used in running-locking fashion to complete the posterior inner layer.
3. The posterior inner layer is joined together and tied to the anterior portion of the anastomosis with the second 3-0 Polysorb™ suture. The anterior inner layer remains unlocked (Fig. 10.5).

10.6 Outer Anterior Row of PJ [14, 15]

1. An outer anterior row of interrupted 3-0 silk sutures is placed in a vertical mattress fashion to complete the pancreatic anastomosis. The vertical sutures are designed to roll the jejunum over the anterior inner layer, and the tension is dispersed by crossing each suture over

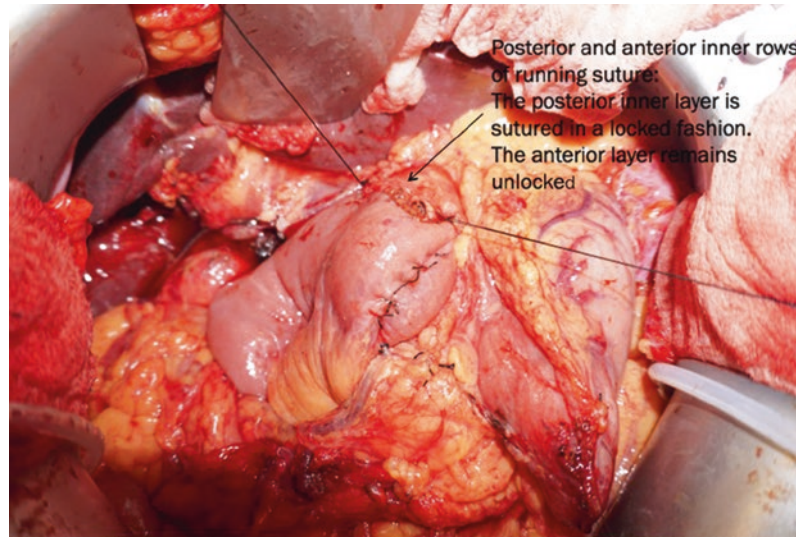

Fig. 10.5 The posterior inner layer is joined together and tied to the anterior portion of the anastomosis with the second 3-0 Polysorb™ suture. The anterior inner layer remains unlocked

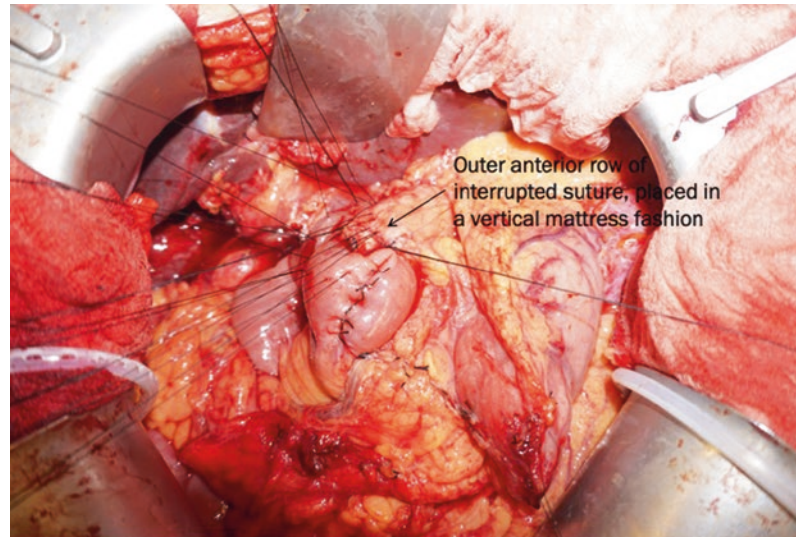

Fig. 10.6 An outer anterior row of interrupted 3-0 silk sutures is placed in a vertical mattress fashion to complete the pancreatic anastomosis. The vertical sutures are designed to roll the jejunum over the anterior inner layer, and the tension is dispersed by crossing each suture over the preceding suture

the preceding suture while they are being tied (Fig. 10.6).

2. Figure 10.7 demonstrates the completed invaginated PJ.

10.7 Hepaticojejunostomy (HJ) [14, 15]

1. The HJ is constructed several centimeters distal to the PJ in an end-to-side fashion, with a single layer of interrupted 5-0 polydioxanone (PDS®) sutures.

10.8 Duodenojejunostomy (DJ) [14, 15]

1. The DJ is constructed in a two-layer hand-sewn technique—20–40 cm distal to the HJ.

10.9 Drainage and Closure [14, 15]

1. Two Jackson-Pratt drains are positioned on either side of the abdomen as a precaution against the occurrence of fistula. The right

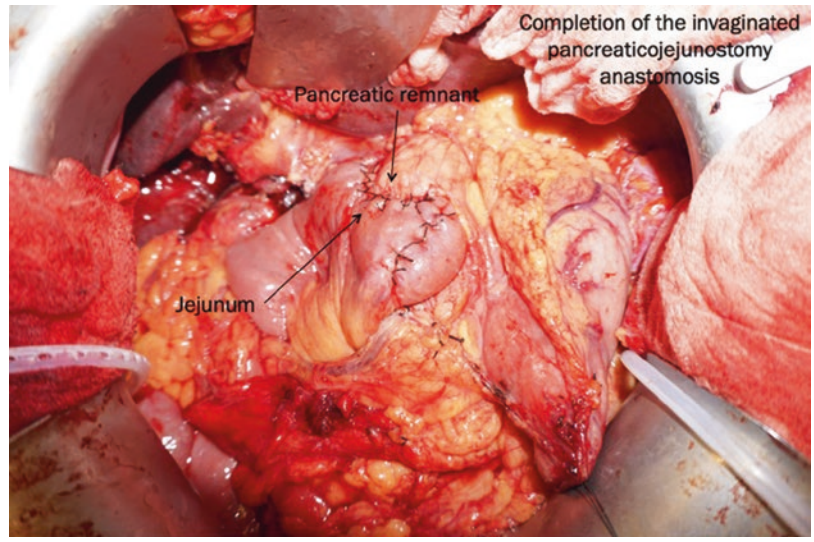

Fig. 10.7 The completed invaginated PJ is demonstrated

drain is positioned within the subhepatic space, posterior to the right upper quadrant (RUQ) jejunal loop, which we term the neo-duodenum. The left drain is placed posterior to the stomach through the gastrocolic ligament and superior to the PJ. #2 Nylon suture in a running fashion is used to close the fascia, and the subcutaneous tissue and skin are closed with 3-0 and 4-0 Vicryl™ sutures, respectively.

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11 Through-and-Through Transpancreatic Duct-to-Mucosa (Blumgart) Pancreaticojejunostomy

Rohit Chandwani and William R. Jarnagin

11.1 Introduction (Literature Review)

Pancreatic fistula (PF) remains a common and significant source of postoperative morbidity in patients undergoing pancreaticoduodenectomy. While mortality following the Whipple procedure has improved substantially to rates close to 1% in several large Western centers [1, 2], morbidity remains high with rates of 30–40% [3]. Whereas for most operative interventions surgical complications typically include anastomotic leak, hemorrhage, and wound infection, it is the pancreatic leak or fistula that is the most common source of perioperative morbidity. Classified by the International Study Group on Pancreatic Fistula (ISGPF) criteria, the clinically relevant Grade B and C fistulae historically required reoperation and now are commonly addressed by percutaneous or endoscopic techniques [4]. These technical advances notwithstanding, pancreatic fistulae remain an intractable source of morbidity following pancreaticoduodenectomy.

The risk factors for pancreatic fistula have been well studied. These include pancreas-specific features [type of pathology, soft texture to the pancreatic parenchyma, or small duct size (often occurring when there is a lack of antecedent pancreatic ductal obstruction)] and patient-specific features [intraoperative blood loss, poor blood supply, diabetes, obesity] that either make the technical reconstruction or wound healing, respectively, considerably more challenging [5]. In patients with both pancreas- and patient-specific risk factors, the incidence of clinically significant postoperative pancreatic fistula approaches 30% [6]. However, even in those patients with low fistula risk scores, the risk of PF remains upward of 6% [7].

Several approaches have been undertaken to prevent pancreatic fistulae. The pharmacologic approach has sought to minimize pancreatic secretions, typically through the use of somatostatin analogues such as octreotide. The extensive data on octreotide are mixed, with a recent Cochrane review suggesting a decreased rate of pancreatic fistula (RR 0.66; 95% CI 0.55–0.79; $n = 2206$) and postoperative complications (RR 0.70; 95% CI 0.61–0.80; $n = 1903$) with the use of octreotide. These findings, however, were not significant in those studies using ISGPF criteria to determine clinical relevance (RR 0.69; 95% CI 0.38–1.28; $n = 292$) [8]. Pasireotide, a somatostatin analog with a longer half-life than octreotide, was shown in a randomized controlled trial performed at our institution to decrease the incidence of clinically significant pancreatic fistulae following pancreaticoduodenectomy as compared

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to placebo (10% vs. 21%; $p = 0.04$) [9]. Several subsequent studies have since suggested that this intervention is cost-effective [10–12].

Other factors that have been evaluated have been the type of suture material, the use of fibrin sealants (to better secure the pancreaticojejunal anastomosis), and the use of external and internal pancreatic stents. One retrospective comparison study has evaluated the outcomes following the use of absorbable and nonabsorbable sutures, finding no difference between suture types [13]. Similarly, fibrin sealants appear to offer no benefit in terms of perioperative morbidity and mortality, with an incidence of pancreatic fistula following pancreatic resection across several randomized studies of 29.6% when fibrin sealants were used and 31.0% in control groups (RR 0.93; 95% CI 0.71–1.21; $p = 0.58$) [14]. With respect to stent placement, internal stenting across the pancreaticojejunal anastomosis does not reduce the rate of PF formation [15], but there does appear to be a risk reduction with externalized stents (6% stent vs. 22% no stent; $p = 0.04$) [16]. However, systematic review does not support the use of either external or internal stenting [17].

Perhaps the most abundantly researched in the effort to lower the incidence of pancreatic fistulae has been the specific technique of pancreatic anastomosis. Among the many established approaches are the typical duct-to-mucosa pancreaticojejunostomy (with or without parenchymal sutures), invagination into the jejunum, and pancreaticogastrostomy [18]. Despite extensive study, the literature fails to offer clarity on which approach is associated with improved outcomes. Recent randomized controlled trials have suggested a superiority of pancreaticogastrostomy over pancreaticojejunostomy when subjected to meta-analysis with rates of PF reduced from 18.7% to 11.2% [19]. Another contemporaneous meta-analysis showed similar findings across seven randomized controlled trials, with a reduction in PF among pancreaticogastrostomy patients (10.6% vs. 18.5%; $p = 0.0002$). Subgroup analysis restricted to those studies in which ISGPF criteria were used also showed a significant difference (8.3% vs. 20.5%; $p < 0.00001$) [20]. Additional meta-analyses have also suggested a decreased incidence of PF with pancreaticogastrostomy and a modest impact on overall morbidity [21–23]. However, a more recent multicenter German randomized controlled trial (RECOPANC) included 320 patients in an intent-to-treat analysis, finding no difference in the incidence of Grade B/C pancreatic fistulae between pancreaticogastrostomy and pancreaticojejunostomy (20% vs. 22%; $p = 0.617$) [24], and a greater number of postoperative hemorrhage in the PG group. In the end, while the preponderance of data suggests that pancreaticogastrostomy should be preferred over pancreaticojejunostomy, it is crucial to note that the pancreaticojejunostomy techniques employed in the aforementioned studies were invariably heterogeneous.

Indeed, the outcomes following alternative methods of pancreaticojejunostomy can be quite varied. In an early randomized trial comparing invagination to a duct-to-mucosa anastomosis, the former was associated with a lower rate of pancreatic fistula formation (12% vs. 24%; $p < 0.05$) [25]. This contrasts with the prior randomized trial from Italy showing no difference in outcomes between the two techniques, including a similar incidence of pancreatic fistula (13% for duct-to-mucosa anastomosis and 15% for invagination; p = ns) [26]. Additional trials showing conflicting data regarding these methods have since followed [27], and a recent meta-analysis showed no significant difference (OR = 1.23 for duct-to-mucosa vs. invagination; $p = 0.38$) across the published studies [28].

At our institution, we utilize an altogether different reconstructive method—the Blumgart pancreaticojejunostomy—that combines a duct-to-mucosa anastomosis with transpancreatic sutures. Because the jejunum is imbricated over the entire transected pancreatic parenchymal surface, this technique essentially couples a duct-to-mucosa anastomosis to the proposed advantages of invagination. Performed over the last 25 years at our institution and by hundreds of trainees across the world, this technique has become our preferred means of pancreaticojejunal anastomosis. Here we discuss the critical aspects of the surgical technique and review the literature regarding its use in the reconstruction following pancreaticoduodenectomy.

11.2 Surgical Technique

Resection is performed in the standard fashion, with removal of the head of the pancreas and the duodenum. Pylorus preservation can be performed as dictated by the indication for operative intervention. During pancreatic transection, four stay sutures—typically consisting of a 3-0 monofilament absorbable suture (such as PDS)—are placed at the superior and inferior aspect of the pancreas on both sides of the intended line of transection. Two of these remain on the pancreatic remnant following extirpation of the specimen. At this point, the remnant is prepared by dissecting it free of the splenic artery and vein for a length of 1–2 cm. The jejunal limb is then brought through a defect in the transverse mesocolon that is created to the right of the middle colic vessels, such that the proximal jejunal end sits to the right of the inferior aspect of the pancreatic remnant. Absorbable stay sutures are placed in the jejunum approximately 10–15 cm apart—representing the full extent of the jejunum incorporated into the future anastomosis—in order to splay out the small intestine during the creation of the retrocolic pancreaticojejunostomy.

The critical component of the through-and-through (Blumgart) approach is the careful placement of several transpancreatic U-sutures. At our institution, we use 3-0 braided absorbable sutures (such as VICRYL) that are placed in interrupted fashion beginning at the superior aspect of the pancreatic remnant. The first suture is placed adjacent to the superior 3-0 PDS stay suture, taking care to avoid the pancreaticoduodenal vessels. As with all the transpancreatic sutures, this stitch is first placed in the anterior surface of the pancreas and brought out the posterior aspect. A horizontal seromuscular stitch in the jejunum—approximately 1 cm of travel along the longitudinal axis of the bowel and well-posterior to the anticipated duct-to-mucosa anastomosis (i.e., closer to the posterior mesentery)—is then placed, with the stitch then taken back through the pancreas posterior to anterior, exiting about 0.5 cm from the initial entry of the stitch on the anterior surface. Six of these 'U' horizontal mattress stitches are placed—three cranial and three caudal to the pancreatic duct—taking extreme care on the interior two stitches to avoid placing the stitch through the duct itself. (A plastic stent can be inserted into the duct to avoid this issue.) Each stitch travels along the length of the bowel, incorporating a total of 8–10 cm of jejunum into the anastomosis. The stitches are not tied, and the needles are left on all six stitches; importantly, the jejunum is not approximated to the pancreas at this time. It is critical in the placement of these sutures to maintain organization for later completion (Fig. 11.1).

The duct-to-mucosa anastomosis is then performed. A small enterotomy using the needlepoint on the electrocautery is made in the jejunum, between the third and fourth 'U' stitches and exactly on the antimesenteric side of the jejunum. The full anastomosis will usually consist of 6–8 interrupted monofilament absorbable sutures (usually 4-0 or 5-0 PDS) for larger ducts and 4–6 sutures for smaller ducts. Invariably, the first stitch is placed in the 6 o'clock position on the inside of the pancreatic duct, exiting through the posterior aspect of the remnant and then full thickness through the jejunum, from the serosa to the lumen

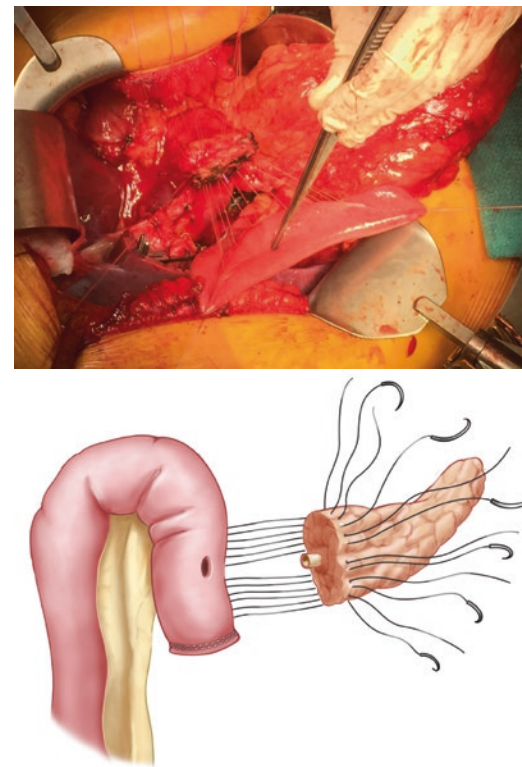

Fig. 11.1 Placement of transpancreatic sutures

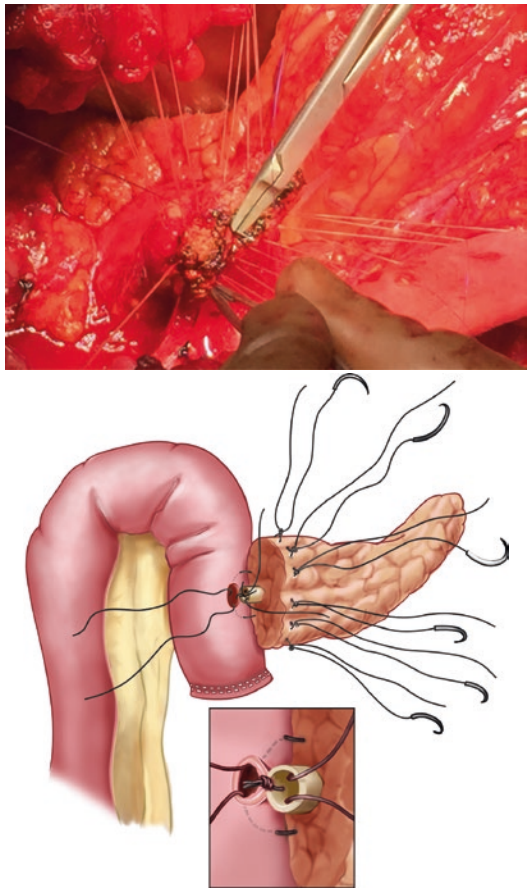

Fig. 11.2 Placement of posterior row of duct-to-mucosa sutures

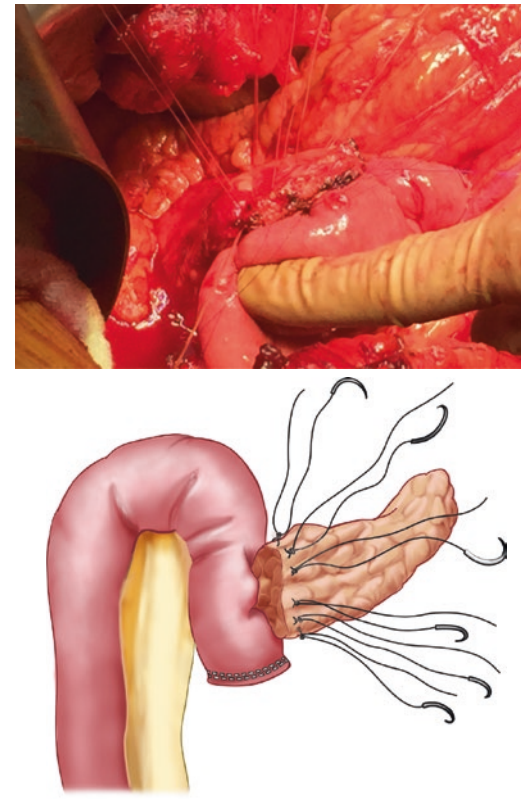

Fig. 11.3 Apposition of the pancreas to the jejunum

(Fig. 11.2). Adjacent sutures are then placed in the 3 and 9 o'clock positions (for small ducts) or in the 4 and 8 o'clock positions (for normal or larger ducts). As with the initial duct-to-mucosa suture, the needle is first passed from the lumen of the pancreatic duct out the posterior parenchyma and then from serosa to mucosa on the jejunal side.

At this point, the jejunum is parachuted down to the pancreatic remnant, and the transpancreatic U-sutures are tied (with the needles left on). This approximates the jejunum to the posterior face of the pancreatic remnant and decreases tension on the stitches of the duct-to-mucosa anastomosis. The 6 o'clock duct-to-mucosa suture is then tied, followed by the additional posterior stitches (4 and 8 o'clock or 3 and 6 o'clock, as dictated by duct size) (Fig. 11.3). To complete the duct-to-mucosa anastomosis, the anterior set of stitches are then placed in similar fashion —except the 12 o'clock stitch, for which the needle is first placed on the anterior pancreatic parenchymal surface, brought through the duct and then from mucosa to serosa on the jejunal side. These sutures are tied as they are placed.

With the duct-to-mucosa inner layer complete, attention is turned to the completion of the transpancreatic sutures. The needle of the most cranial transpancreatic suture is taken, and two seromuscular bites are taken through the jejunum. The first of these is transversely from the posterior mesenteric side (incorporated in the first part of the anastomosis) to the anterior mesenteric side. The second is parallel to the longitudinal axis of the bowel. This represents the corner transpancreatic U-suture, and the stitch is tied so that the jejunum forms a wrap over the anterior surface of the pancreas at its most superior aspect. The next four transpancreatic sutures are completed by

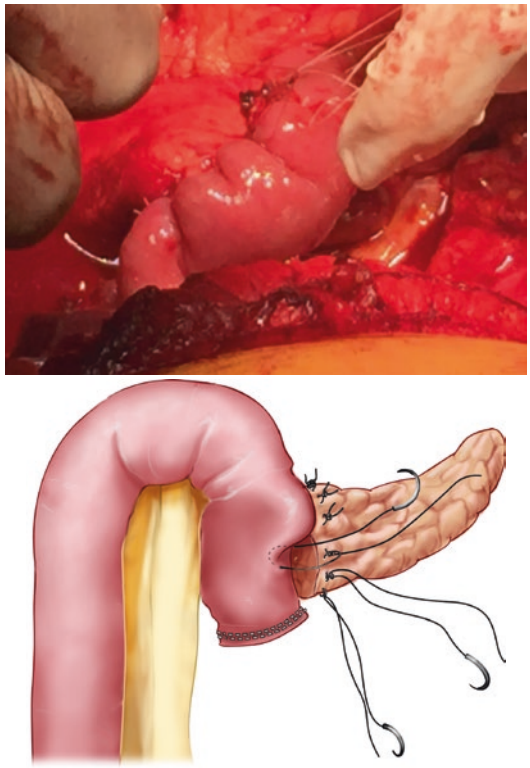

Fig. 11.4 Placement of anterior seromuscular jejunal sutures

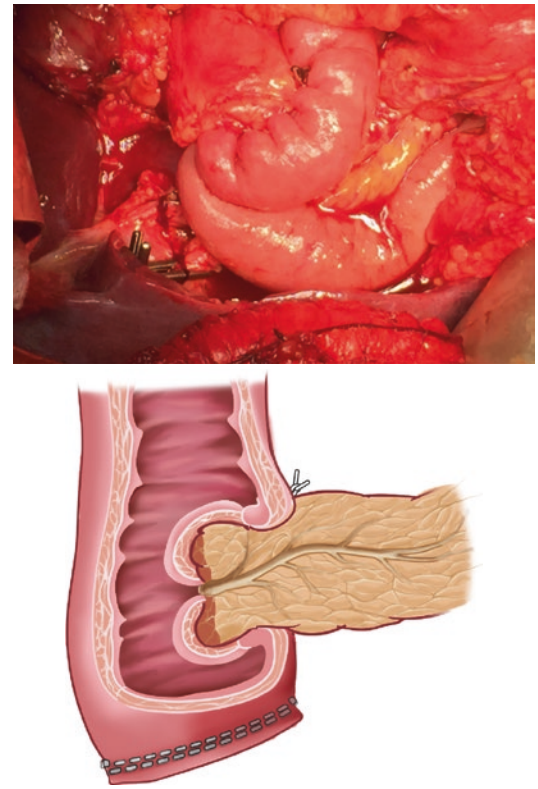

Fig. 11.5 Completed Blumgart pancreaticojejunostomy

taking 1 cm travel seromuscular stitches in the jejunum (again along the longitudinal axis of the bowel), close to the anterior mesentery so that there is adequate distance from the duct-to-mucosa anastomosis. Each of these is tied so that the jejunum is brought over the anterior surface of the pancreatic parenchyma (Fig. 11.4). The last transpancreatic suture is also a corner stitch with two bites taken—the first is longitudinally on the bowel and the second transversely such that the final needle exit on the jejunum is 0.5 cm from the suture taken through the posterior surface of the jejunum.

The final result of the anastomosis is depicted in Fig. 11.5, showing the entire transected surface of the pancreas completely covered by jejunal serosa. While the Cattell-Warren pancreaticojejunostomy and most other technical approaches do also cover the transected surface, the Blumgart anastomosis differs in that the pancreatic remnant should appear imbricated into the jejunum.

11.3 Results

As with the multitude of measures described in the foregoing, the through-and-through duct-to-mucosa (Blumgart) pancreaticojejunostomy has been the subject of extensive clinical investigation. In a multi-institution report of 187 consecutively treated patients, the Blumgart pancreaticojejunostomy described herein was associated with a 6.9% incidence of Grade B and C pancreatic fistula (by ISGPF criteria). Perioperative mortality was low at 1.6%, and the incidence of reoperation was 5.3%; notably, neither mortality nor reoperation occurred in a patient with a postoperative pancreatic fistula [29]. There was a 13.4% incidence of Grade A pancreatic fistula not altering clinical management. Compared with other retrospective studies employing the ISGPF criteria, this report compares favorably with the results of other technical approaches. Similarly, a group in India applied

this technique in 98 consecutive patients, finding an incidence of Grade B and C pancreatic fistula of 7.14%, with only one patient requiring re-exploration due to leak [30]. As various contemporaneous retrospective studies examining the outcomes of other reconstruction techniques have shown an incidence of Grade B and C fistulae of 10–15%, the outcomes following Blumgart pancreaticojejunostomy in these two studies represent a significant improvement [31, 32].

Several studies have provided higher quality evidence by comparing the Blumgart technique directly with other technical methods. One such study employed a before-after retrospective design from a single institution in Germany examining the outcomes following the Blumgart pancreaticojejunostomy versus a Cattell-Warren anastomosis. The Blumgart anastomosis was performed in the fashion described herein, while the latter consisted of interrupted anterior and posterior rows of sutures between the seromuscular jejunum and the anterior and posterior pancreatic capsule, respectively (in conjunction with a duct-to-mucosa anastomosis). The authors of this study observed a statistically significant decrease in operative time and a trend toward decreased blood loss in the Blumgart anastomosis group. Importantly, the rate of surgical complications and the rate of Grade B and C pancreatic fistula were statistically significantly lower (4% vs. 13%; $p = 0.032$). Finally, in a multivariate analysis, the type of anastomosis (Blumgart vs. Cattell-Warren) was a significant predictor of both major local complications and systemic complications [33]. In another line of evidence, a second German group published similar findings in a randomized study comparing a transpancreatic mattress suture anastomosis to the conventional Cattell-Warren pancreaticojejunostomy. Their technique, representing a variation on the Blumgart anastomosis, employed transpancreatic U-sutures, not in conjunction with a duct-to-mucosa anastomosis, but with the invagination of the entire cut surface of the pancreas into a large jejunal opening; in their hands, there was a trend toward fewer complications in the group using transpancreatic mattress sutures with invagination compared to a group in whom Cattell-Warren anastomoses were performed [34]. In both studies, the authors theorize that the shear forces on the pancreatic parenchyma are lessened by the transpancreatic sutures, as knot-tying compresses the full-thickness parenchyma rather than generates perpendicular force that in the soft pancreas tears through the tissue.

More recently, further evidence to support the use of the Blumgart anastomosis has been offered by additional comparison studies. In one, a Japanese group compared the Kakita method (interrupted full-thickness pancreatic sutures + a duct-to-mucosa anastomosis) to the transpancreatic mattress method described here. Of note, externalized pancreatic stents were employed in all patients with a pancreatic duct of less than 3mm in diameter. In this single-institution matched historical control study with 120 patients in each arm, the Blumgart technique was associated with a significantly lower rate of Grade B and C pancreatic fistula (2.5% vs. 36%; $p < 0.001$), shorter duration of drain placement, and shorter postoperative stay [35]. Another Japanese group also examined in a retrospective fashion the outcomes of the Kakita method with the Blumgart anastomosis, finding a lower rate of Grade B and C fistula in the through-and-through mattress method (20.5% vs. 37.2%; $p = 0.033$) [36]. It should be noted that the rate of clinically significant fistulae was quite high in this report and does well exceed those described in Western centers for most methods of reconstruction.

An important piece of evidence has also been recently offered from a Taiwanese group comparing the outcomes of the Blumgart anastomosis with that of pancreaticogastrostomy. Given that several studies have compared various methods of pancreaticojejunostomy with pancreaticogastrostomy and that there is suggestion that the latter may be superior, this comparison is an important one. In a retrospective analysis of a prospectively maintained database, the Taiwanese study examines 206 matched patients undergoing pancreaticoduodenectomy and either Blumgart pancreaticojejunostomy or pancreaticogastrostomy. In this series, the former was associated with a decreased incidence of clinically relevant

pancreatic fistulae (7% vs. 20%; $p = 0.007$), shorter hospital stay, and decreased perioperative mortality (0% vs. 4.9%; $p = 0.03$) [37]. Taken together, the largely retrospective series throughout the literature do concur that there are fewer complications, and specifically a decreased rate of clinically significant pancreatic fistulae, when the method of reconstruction is that described here.

Despite the foregoing, there remains a paucity of high-level clinical evidence to delineate the optimal method of pancreaticojejunostomy. To address this issue, the PANasta trial has been announced. A multicenter, double-blinded, randomized controlled trial, PANasta, aims to evaluate if the Blumgart pancreaticojejunostomy is superior to the Cattell-Warren anastomosis. The primary endpoint of the study will be the rate of pancreatic fistula, and secondary endpoints include mortality, surgical complications, nonsurgical complications, hospital stay, and completion of adjuvant chemotherapy. Aiming to enroll 253 patients per study arm, the study is powered to detect a 10% absolute risk reduction in the rate of pancreatic fistula and is expected to be completed following an enrollment period of 3 years and a 1-year follow-up [38]. However, in the absence of level I clinical evidence, the literature supports the use of the transpancreatic Blumgart anastomosis over alternative methods of pancreaticojejunostomy with respect to clinical outcomes.

Final considerations in support of the Blumgart anastomosis are the technical advantages for the operating surgeon. The transpancreatic mattress method provides a suitable window for creation of the duct-to-mucosa portion of the anastomosis, as the jejunum is not apposed to the cut surface of the pancreas until the latter is completed. In the Cattell-Warren anastomosis, the jejunum is in apposition with the pancreas when the posterior row of duct-to-mucosa sutures is placed, rendering visualization more difficult. Finally, the transpancreatic method has in our institutional experience proven to be facile to teach to trainees. That many MSKCC-trained surgeons continue to employ this method of reconstruction described herein supports the notion that the anastomosis is reproducible in the hands of surgeons both nationally and internationally.

Conclusions

As surgical complications and specifically pancreatic fistula following pancreaticoduodenectomy are a considerable source of perioperative morbidity, a large body of clinical research has centered on the various pharmacologic and technical measures that can be employed to decrease the incidence of postoperative PF. While the role for several interventions is limited by a paucity of clinical evidence, there are several reports supporting the use of a through-and-through transpancreatic duct-to-mucosa pancreaticojejunostomy, also known as the Blumgart anastomosis. Technically facile, this technique is associated with lower rates of pancreatic fistula across several institutions and in comparison to alternative methods. In the absence of high-level clinical evidence, there remains of preponderance of data to support widespread use of the Blumgart anastomosis as the reconstruction method of choice in patients undergoing pancreaticoduodenectomy.

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Binding Pancreaticojejunostomy: How I Do It

12

Jiang Tao Li, Shu You Peng, and Yuan Quan Yu

12.1 Introduction

Pancreatic leakage after pancreaticoduodenectomy (PD) is the main complication which contributes to prolonged hospitalization and increased costs significantly, even causing death. The incidence of pancreatic leakage of conventional pancreaticojejunostomy ranged from 9.9 to 28.5%, and the mortality due to pancreatic fistula was as high as 20–50% [1]. The efforts have been made to minimize the occurrence of this complication after PD. Bundles of techniques have been proposed for the reconstruction of pancreatic digestive tract continuity, while the best procedure is still controversial.

The leakage from a pancreatic digestive anastomosis can be developed at a site where the needle inadvertently penetrates the pancreatic ductule, or a suture cuts the fragile pancreatic parenchyma on suturing or on tying the knot. The minor leak of pancreatic juice gradually leads to a gross anastomotic leakage as a consequence of autodigestion around the anastomosis. Based on this hypothesis, we designed a novel technique of pancreatic digestive reconstruction, which was reported as intraseromuscular sheath pancreaticojejunostomy for the first time in 1996 [2]. Because of the substitution of suture with binding, this surgical technique has been named as binding pancreaticojejunostomy (BPJ) finally. [3, 4] Till 2003, 227 consecutive patients underwent using this technique; none of the cases developed a pancreatic anastomotic leak [5].

With the increasing of clinical applications and the development of surgical technique of binding pancreatic digestive reconstruction, we simplified the surgical procedure in 2002 [6, 7]. In 2003, the reliability of BPJ was verified by animal experiment [8]. In 2004, we evaluated the advantage of BPJ and the appropriate degree of tightness of binding from the view of tolerance pressure of the anastomotic stoma [9]. Considering to the disadvantage of BPJ, in 2009 we developed binding pancreaticogastrostomy [10]. In 2011, binding pancreatic duct-to-mucosa anastomosis [11] and end-to-side BPG was developed [12], respectively. Therefore a series of binding pancreatic digestive reconstructions have been developed, and the application is expanded depending on the characteristics of the pancreas, even in the laparoscopic surgery, while the rate of pancreatic anastomotic leak remains low [13, 14].

From 1996 up to now, a total of 172 publications have been searched via the Wanfang Data (Chinese database), Web of Science, and PubMed using the term "binding pancreaticojejunostomy," including Chinese and English.

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12.2 Surgical Procedure [4, 5, 15, 16]

12.2.1 Preparation of the Jejunum for Binding Anastomosis

The stump of the jejunum is everted for 3 cm; this can be achieved by suturing the jejunal cut edge to a site at the jejunum 6 cm from the edge (Fig. 12.1). Two such sutures are done and tied knots loosely, rendering 3 cm of the jejunum everted with its mucosa exposed, which then is destroyed by electric coagulation or by 10% carbolic acid and rinsed immediately with 75% alcohol and normal saline (Figs. 12.2 and 12.3).

12.2.2 Preparation of the Pancreatic Stump

The residual end of the pancreas is isolated for a length of 3 cm; usually two to three small branches of splenic vein (SV) between the pancreas and the splenic vein were divided and ligated. After the adequate isolation, the isolated pancreatic remnant can be lifted upward; thus the splenic artery and vein can be seen and separated by a small area of pancreas which is the point for fixing the posterior cut edge of the jejunum.

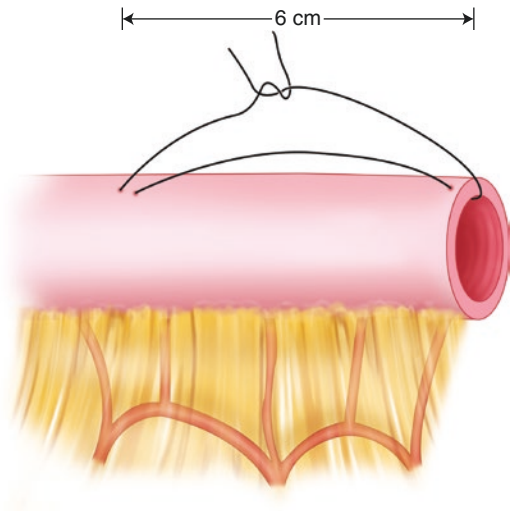

Fig. 12.1 The cut end of the jejunum is prepared for eversion

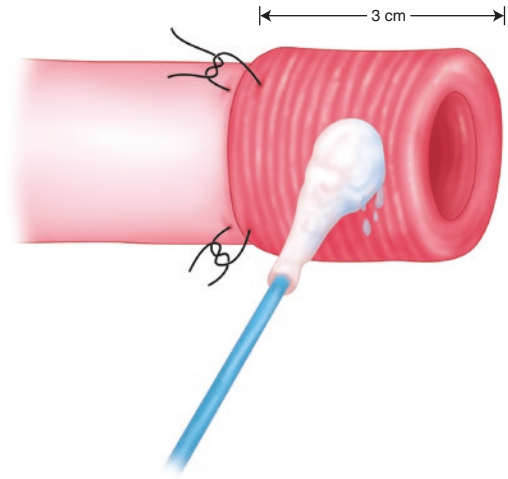

Fig. 12.2 The everted mucosa is daubed with 10% carbolic acid and rinsed immediately with 75% alcohol and normal saline

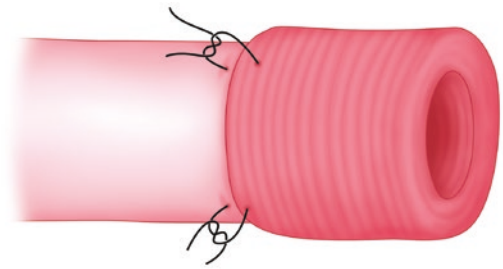

Fig. 12.3 A rim of intact mucosa is left for anastomosis

12.2.3 Two Stumps Sutured

The end of the residual pancreas and everted jejunum are brought together and sutured continuously or intermittently in a circular fashion; care is taken to suture the mucosa only and to avoid penetrating the muscular and serosa layers of the jejunum. The anterior or posterior lip of the pancreatic duct should be involved in the anterior or posterior row of sutures, respectively, whenever possible (Fig. 12.4).

12.2.4 Intussusceptions

The two sutures on the everted jejunum are removed before the everted jejunum stump is restored to its normal position, so as to wrap over the residual end of the pancreas. The cut end of the jejunum by a few stitches is fixed onto the pancreas. Special attention is paid to the posterior fixing point as mentioned above.

12.2.5 Binding

At 1.5–2 cm from the cut edge of the jejunum, a 3-0 absorbable tie is looped around the jejunum circumferentially together with the intussuscepted pancreas (Fig. 12.5). The tip of a hemostatic clamp can be passed underneath the binding ligature to verify the tightness. The blood supply to the jejunum distal beyond the binding ligature is ensured by preserving several vessels for that segment of jejunum. The thread for making the binding ligature is placed through a hole at the jejunal mesentery between the last two groups of vessels near the cut edge.

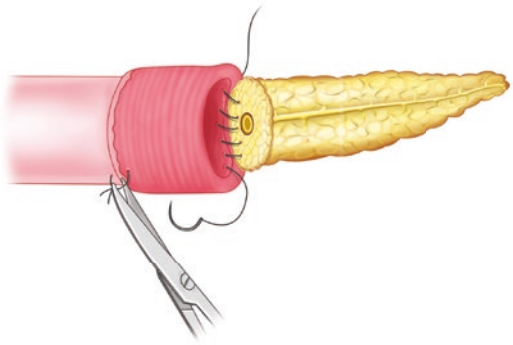

Fig. 12.4 Mucosa and muscularis mucosa of the jejunum are sutured to the cut end of the pancreas

12.2.6 Jejunostomy

When the anastomosis was finished, a catheter is inserted into the jejunum through the site where choledochojejunostomy is intended to be constructed, for injection of saline to test for a watertight closure. Jejunostomy through the defunctionalized loop with a catheter left in about 12 cm distal to the choledochojejunostomy is performed for decompression or X-ray study postoperatively.

12.2.7 Drainage

A Jackson-Pratt drainage tube is placed near the pancreatic digestive anastomosis. The volume and amylase content of the drainage fluid are measured on day 1 and 3 after operation. The definition of pancreatic leakage was used according to the International Study Group for Pancreatic Fistula (ISGPF), pancreatic fistula is defined as output via an operatively placed drain

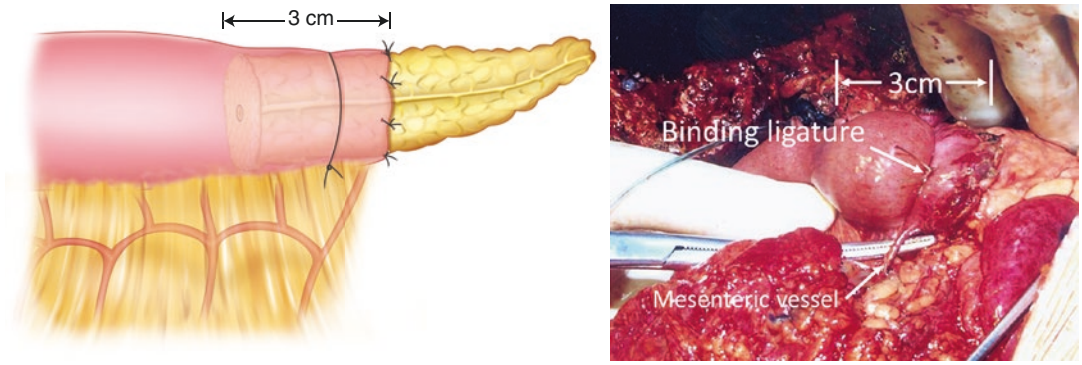

Fig. 12.5 The remnants of the pancreas in the lumen of the jejunum are looped and ligated together

(or a subsequently placed percutaneous drain) of any measureable volume of drain fluid on or after postoperative day 3, with an amylase content greater than 3 times the upper normal serum value [1].

12.3 Comment

Pancreaticojejunostomy anastomotic leak rate of 0% was reported at the initial series with BPJ technique [16]. Strictly speaking, pancreaticojejunostomy anastomotic leak rate should be referred to the grade B or grade C pancreatic fistula depending on the ISGPF. The mechanism of BPJ including (1) the sutures of jejuna is only limited to the jejunal mucosa, not different from traditional reconstruction which the whole layer of jejunal was sutured; thus, no possibility of needle hole leakage can be developed; this is called the first line of defense. (2) The jejunum mucosa which secretory function was destroyed is wrapped over the residual end of the pancreas; this close contact could accelerate the healing between the jejunum and the pancreas. Once the leakage was presented, like a circular defense line, a binding ligature can prevent the pancreatic juice from leaking on the gap between these two organs. (3) Beyond the binding ligature, one branch of mesenteric vessel to the jejunal cut end should be preserved so there would be enough blood supply for the anastomosis site. The 3 cm of remnant pancreas usually was isolated, the blood supply of the cut end of pancreas was also guaranteed, and the abundant blood supply for the jejunal and the remnant pancreas is the prerequisite of healing for pancreaticojejunostomy. [17] These three principles are the main mechanisms for BPJ compared with the traditional pancreaticojejunostomy.

One of the tricks of BPJ is how to define the tightness of the binding ligature by different surgeons. If the tie is too loose, the pancreatic juice is easy to leak from anastomosis site. If the tie is too tight, inadequate blood supply to the distal pancreas will be developed and easy to compress the pancreatic duct by tight ligature. Depending on the results of our previous animal study, the anastomosis for a watertight seal could be tested by instilling saline dyed with methylene blue at a pressure of 40 cmH_2O [9]. A dent of 1–2 mm can be preserved in the jejunum under the ligature, so the tip of a vascular clamp should be able to pass; close contact between the jejunum and the remnant pancreas can be developed, and ischemic necrosis due to being too tight was avoided. The results of animal experiments showed that no structure pancreatic duct can be formed by this level of tightness of binding ligature [18, 19].

In 2010, a French prospective study conducted by Bue reported a rate of pancreatic fistula of 8.9% including 45 sequential patients with soft pancreas and non-dilated main pancreatic duct using BPJ technique, which is lower than previously published by the same institution (17.6%) [20]. In addition, it is one of the lowest ever published when soft pancreatic parenchyma and non-dilated main pancreatic duct are involved. However, in the situation in which the diameter of cut edge of remnant pancreas and jejunum is not matched, it may be considered as a contraindication for BPJ. In 2011, Yang et al. from China reported a meta-analysis of randomized controlled trials with regard to the methods of reconstruction of pancreatic digestive continuity after PD [21]. In 2014, a Korean research group reported a lower rate of pancreatic fistula using BPJ than that of conventional pancreaticojejunostomy [22]. The results were not associated with the texture of the pancreatic parenchyma or dilatation of the pancreatic ducts. The above study supports and reproduces the excellent results of Peng's BPJ. In addition, BPJ is also a suitable procedure for patients without pancreatic duct dilatation.

Though none of the anastomosis techniques could be suitable to all kinds of pancreatic remnants and to avoid pancreatic fistula in the past 100 years' history of pancreatic digestive tract reconstruction. As a new technique, BPJ successfully decreased the rate of pancreatic anastomosis fistula. It is verified as a safe procedure for pancreatic anastomosis, especially in case of soft texture of the remnant pancreas. Similarly, like traditional pancreaticojejunostomy, expertise in surgical procedure, operation volume, and other management parameters are also important

factors for BPJ. In China, the practice by broad hospitals including teaching hospitals as well as primary hospitals provides the reliable results using BPJ [23, 24]. We concluded that BPJ is an easy technique for manipulation and popularization.

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13 Pancreaticogastrostomy: How I Do It

R. Mahendran and H. S. Shukla

13.1 Introduction

Pancreaticogastrostomy (PG) was first described by Waugh and Clagett from Mayo Clinic in 1946 [1]. Flaunter et al. popularized the technique and published their series in 1985 [2, 3]. Numerous theoretical and technical advantages are attributed to PG to explain the apparent safety of this procedure [4] including (1) the inactivation of pancreatic enzymes due to the low pH of the gastric lumen and lack of enterokinase in the gastric mucosa; (2) the alkaline pancreatic secretions that may help protect the pancreaticogastric anastomosis against marginal ulceration; (3) the anatomical proximity of the posterior gastric wall to the pancreatic remnant that allows for a very secure anastomosis without tension; (4) the thick gastric wall with its excellent blood supply that holds sutures very well; and (5) postoperative gastric decompression that is easily performed and provides constant removal of pancreatic and gastric secretions, thereby allowing less tension on the pancreaticogastric anastomosis.

PG has commonly been performed either by invagination [5], binding [6] method or by duct-to-mucosa method [7] with some modifications.

Observational individual studies have consistently reported lower overall leak rates with PG when compared to pancreaticojejunostomy (PJ) [8–17]. Single-center nonrandomized studies are often flawed by insufficient sample size, selection bias, lack of uniform definitions of various outcomes such as postoperative pancreatic fistula (PF), and other possible confounding factors such as surgeon's preferences.

Several randomized controlled trials and meta-analysis [18–25] have been conducted to compare the two most preferred techniques (PJ vs. PG). A large majority favor PG over PJ. However a great heterogeneity exists between the studies regarding pancreatic texture, disease pathology, pancreatic duct size, use of somatostatin, etc. The recently published International Study Group of Pancreatic Surgery (ISGPS) position statement [26] also states that "currently, no specific technique can eliminate development of clinically relevant postoperative pancreatic fistula."

Pancreatic intraluminal hemorrhage [25] and pancreatic exocrine insufficiency [27] are however reported to be more common with PG reconstruction than with PJ reconstruction after pancreaticoduodenectomy (PD) for malignancy.

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13.2 Anterior Gastrostomy and PG and Our Experience

This technique of fashioning PG accessed through anterior gastrostomy has been reported by a few authors before with excellent outcomes [13, 28–31]. We have a personal experience with this technique of over 10 years and have published our early results in 2005 [32].

We prefer constructing the PG after classical Whipple's/pylorus-resecting PD by retracting the cut end of the stomach and by creating an anterior gastrostomy after a pylorus-preserving pancreaticoduodenectomy (PPPD).

13.3 Preparation of Pancreatic Stump for PG

The cut end of the pancreas is examined carefully and hemostasis is secured by applying loops of 4'0' PDS sutures. The pancreatic duct is identified, and a small feeding tube is inserted into its lumen. It serves as a guide for the pancreatic duct and helps in placing stiches without accidentally taking a bite in the duct. A 2.5–3 cm length of the pancreatic stump is mobilized from all around taking care on the superior and posterior part to safeguard the splenic vein. The pancreatic stump already has two stay sutures at its two ends. We apply these using 2'0' silk sutures before dividing the neck of the pancreas during PD (Fig. 13.1).

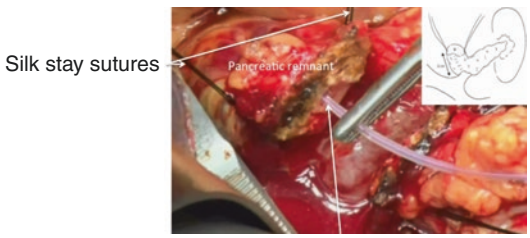


Fig. 13.1 Mobilization of 2.5–3 cm of the pancreatic remnant that is held in stay sutures; temporary nasogastric tube as stent in the pancreatic duct

13.4 Preparation of the Stomach

(a) *For PG after PPD:* An 8-cm-long anterior gastrostomy is made along the longitudinal axis of the stomach. Next a 3-cm-long incision (approximately half the width of the pancreatic remnant) is made perpendicular to the long axis of the stomach, on its posterior wall. Hemostasis is secured (Fig. 13.2).

(b) *For PG after PD:* The clamps on the cut end of the stomach are opened. Anterior cut end of the stomach is retracted. A 3-cm-long incision (approximately half the width of the pancreatic remnant) is made perpendicular to the long axis of the stomach on its posterior wall. Hemostasis is secured at each step (Fig. 13.2).

13.5 Method of PG

A pair of long artery forceps is passed through the posterior gastrostomy, and the stay sutures on either end of the pancreatic remnant are grasped. The mobilized cut end of the pancreatic remnant is then lightly held and steadied as the stomach is pushed around the pancreas. The stump of the pancreas is now within the lumen of the stomach (Fig. 13.3). Interrupted silk 2'0' sutures are applied from within the stomach in single layer. Each stitch is taken through full thickness of the stomach (ensuring that serosa is taken) and a good bite of the pancreatic parenchyma of the pancreatic remnant all around at 1 cm interval (Fig. 13.4). Care is taken not to include the pancreatic duct in the suture line with the help of the identifying nasogastric tube in the duct. Taking bites through the cut end of the pancreatic remnant is avoided. All sutures are next tied avoiding undue tension or tightening (tension causes sutures to cut through the friable pancreas and tightening may result in stump pancreatitis). The cut end of the pancreas protrudes in the lumen of the stomach (Fig. 13.5). The pancreatic duct is checked before closure, using a fine probe, to ensure that the pancreatic duct is patent. Hemostasis is again checked. The anterior gastrostomy is closed in case of PPD and the

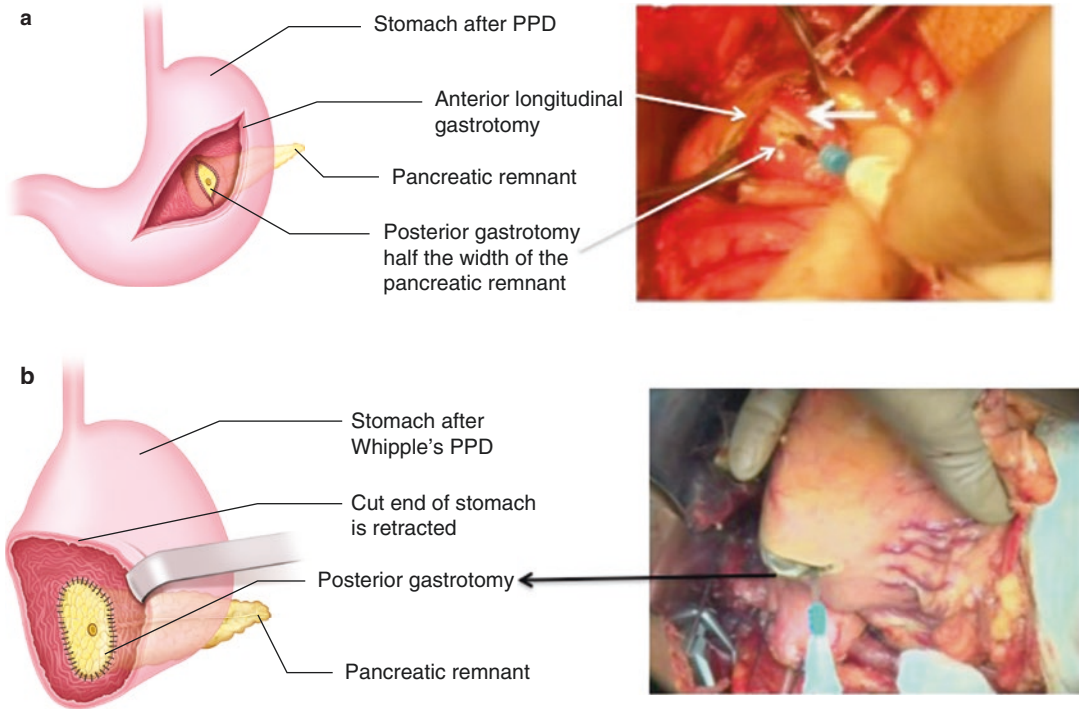


Fig. 13.2 (**a**) Anterior gastrostomy followed by posterior gastrostomy after PPD; (**b**) posterior gastrostomy following pylorus-resecting PD

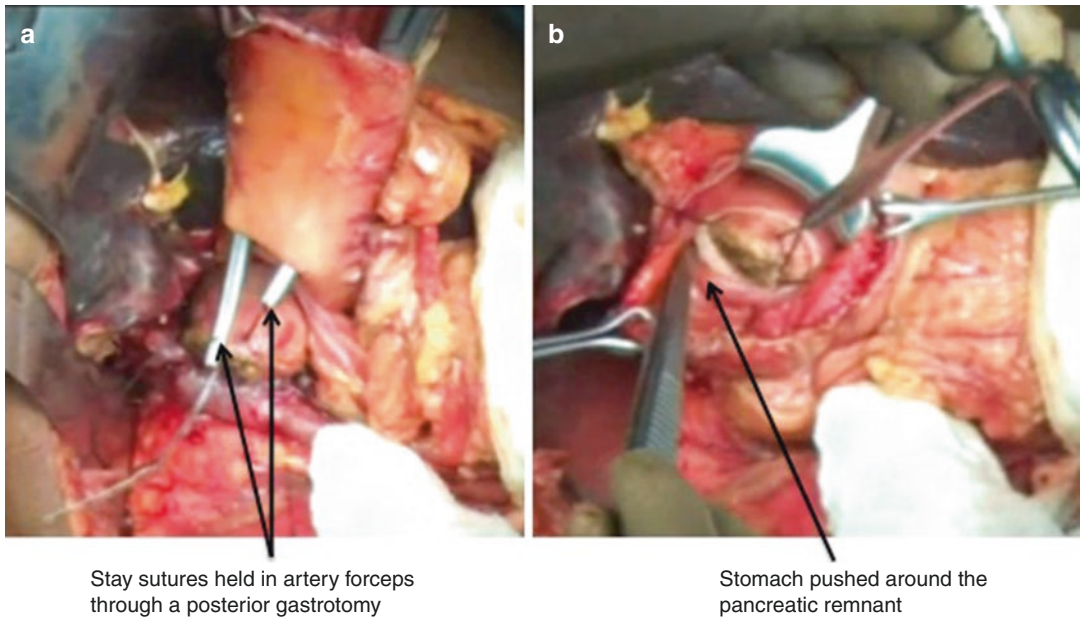


Fig. 13.3 Stay sutures on the pancreatic remnant held in the two artery forceps introduced through the posterior gastrostomy, and then the stomach is pushed around the remnant seating it well inside the stomach lumen

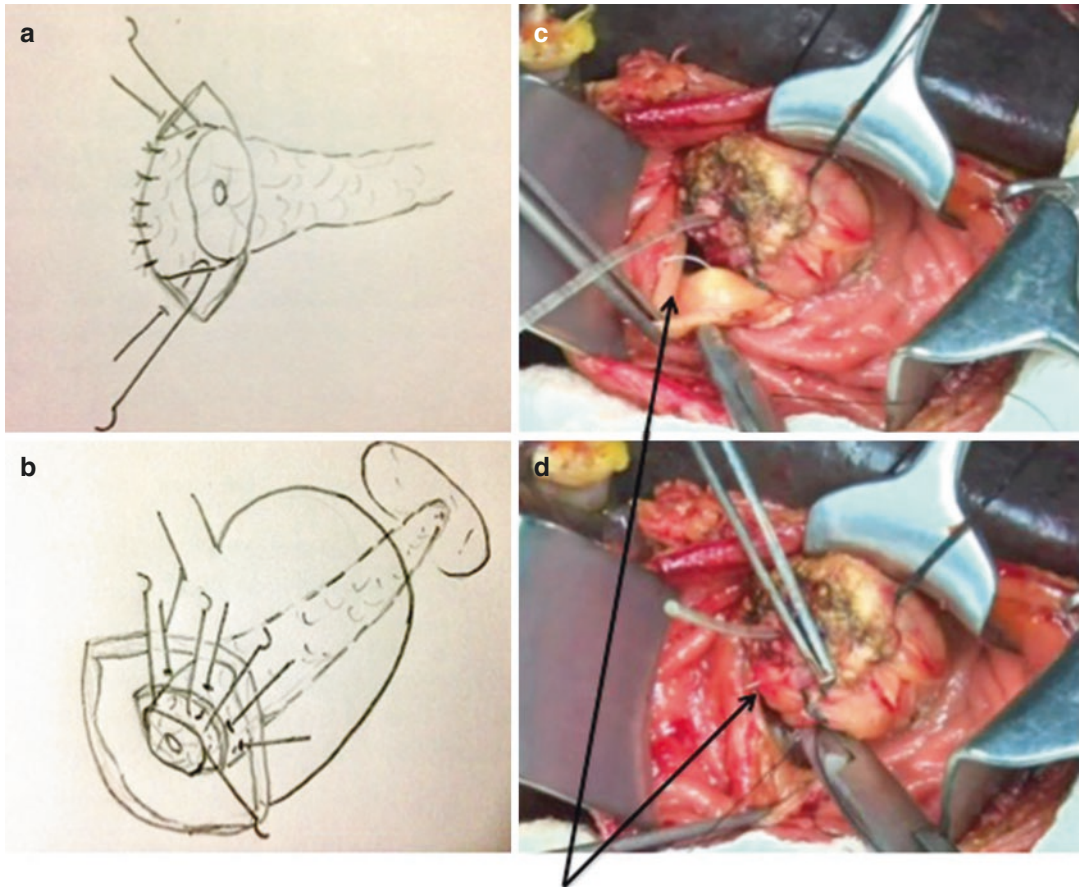
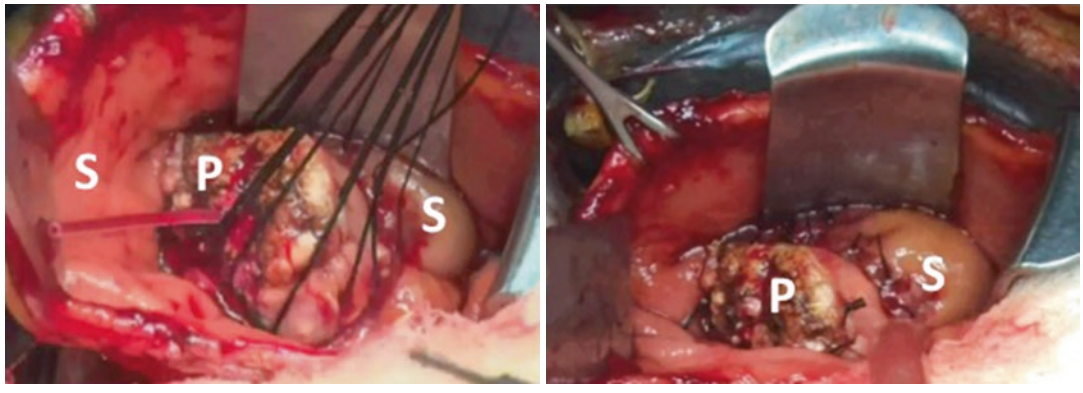


Fig. 13.4 Full thickness bites are taken in the stomach wall and good bites in the pancreatic remnant so that the needle does not come through the cut end of the pancreas



PG completed; P, Pancreatic remnant; S, Stomach

Fig. 13.5 The completed PG with the pancreatic cut end well inside the stomach lumen; hemostasis ensured

duodenal end (or cut end of the stomach in PD) anastomosed to jejunum.

13.6 Discussion

This technique has the following advantages:

1. The anastomosis is carried out under direct vision, is technically easier to construct, and ensures adequate hemostasis of the suture line, thereby preventing suture line hemorrhage that may result in life-threatening postoperative gastrointestinal bleed or predispose to leak.
2. The technique obviates the need for blind invagination of the pancreas that can result in uncontrolled or disproportionate tension on the suture line, accidental inclusion of the pancreatic duct, or undue tightening. It is well known that undue tension at the time of invagination of the pancreatic stump can result in cutting of sutures through the friable pancreas, and stump pancreatitis has been attributed to a tight anastomotic technique or due to accidental occlusion of the pancreatic duct by suture. By testing for ductal patency after construction of PG, which is possible only by the anterior gastrostomy technique, one can cross-check patency.
3. The total operating time required is also reduced.

Ultimately however, the choice of the pancreatic anastomosis PG or PJ largely rests with the surgeon and his experience with a particular technique.

A Fistula Risk Score (FRS) was devised and presented at the American College of Surgeons 97th Annual Clinical Congress, San Francisco, CA, on October 2011 and later published in 2013 [33]. Its aim is to help the surgeon assess the risk of clinically relevant postoperative pancreatic fistula. This original risk score (ranges from 0 to 10) incorporates several operative variables (gland texture, pathology, pancreatic duct diameter, and intraoperative blood loss) that cannot be easily determined prior to a surgical procedure or are difficult to measure accurately, such as intraoperative blood loss. To overcome the shortcomings of the FRS, a modified FRS was developed using the National Surgical Quality Improvement Program (NSQIP) Pancreatic Demonstration Project. The modified FRS (ten-point model) is based on five significant predictors of clinically relevant postoperative pancreatic fistula, namely, sex, BMI, preoperative total bilirubin, pancreatic ductal diameter, and gland texture [34]. These scores may help and guide the surgeons toward the likely complications and hence in determining the anastomotic technique.

Conclusion

This technique of PG is easy, safe, and quick. It ensures a good anastomosis under direct vision.

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14 Pancreaticogastrostomy: How I Do it

Pietro Addeo and Philippe Bachellier

14.1 Introduction

Despite overall improvements in surgical technique and perioperative care, morbidity after pancreaticoduodenectomy (PD) remains high ranging between 30 and 50% [1]. Pancreatic fistula (PF) and its related clinical consequences remain the most dreaded complications after PD with a reported incidence up to 40% [2]. Patient-, pancreas-, and surgeon-related factors have been identified as potential risk factors for PF's occurrence [3]. The ideal pancreaticoenteric reconstruction after PD should be easy to perform, reproducible, and characterized by the lowest fistula rate. Much debate exists about the best reconstruction method after PD. Pancreaticojejunostomy (PJ) and pancreaticogastrostomy (PG) with many technical variants have been described and are actually used in different pancreatic centers. Still, the choice of one method of reconstruction over the other seems to be based on surgeon's experience and preference rather than on robust scientific evidence. However, several retrospective studies and three randomized controlled trials have reported a statistically significantly lower rate of PF after PG compared with PJ [1, 4–8]. Still much criticism exists about the superiority of PG over PJ because other randomized trials showed equality or inferiority of PG compared with PJ. This could be certainly attributed to the high heterogeneity of surgical techniques used to perform PJ and PG in these studies making a homogenous analysis of the results and its applicability in the clinical practice difficult to achieve.

From a theoretical point of view, a PG carries several advantages over PJ. These include the natural contiguity of the pancreatic body to the posterior wall of the stomach, the greater thickness of the gastric wall compared with the jejunum, the excellent blood supply of the stomach, the neutralization of pancreatic enzyme by the acid secretion, and the possibility to easily decompress the PG anastomosis by nasogastric suction [9]. In 1990 Delcore et al. described a double-layer telescoped PG in which 2–3 cm of the pancreatic remnant are telescoped into the pancreatic lumen with a very low rate of PF [10]. These results were further confirmed by a retrospective comparative study that showed that this type of telescoped anastomosis decreased the postoperative PF and re-laparotomy rates compared with PJ [7]. However, the classical PG telescoped techniques require two layers of transfixing sutures between the posterior gastric wall and the pancreatic stump which still can be the source of technical troubles especially in the

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presence of soft and fatty pancreatic remnant. Suturing a friable pancreatic remnant can be the source of postoperative pancreatitis and leaks. Therefore in 2010 we modified the original technique toward the creation of a "sutureless" PG using a purse-string technique [9]. The rationale behind this technique is to reduce all the manipulations of the pancreatic remnant that can be the source of postoperative pancreatitis while preserving the safety of this technique in terms of minimal postoperative PF rate. Later on the technique of the so-called double purse-string PG has been further modified in the "triple purse-string" technique in order to make its fashioning easier and maximize the reproducibility of the technique in other centers. The advantages of this technique rely in its easiness to perform, its reproducibility, and its near zero PF rate.

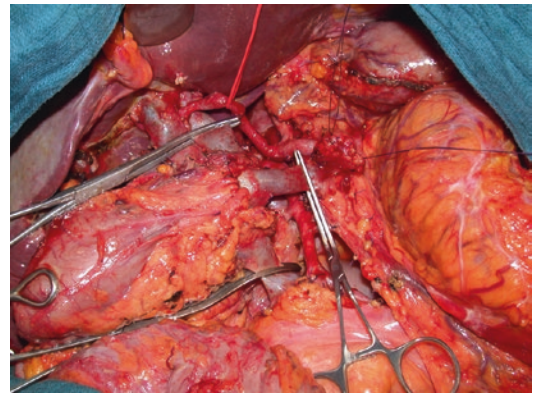

Fig. 14.1 Intraoperative view of a PD with a combined venous and arterial resection; the pancreatic stump has been dissected over the venous and arterial axis for 5 cm. The splenic vein has been reimplanted into the left renal vein

14.2 The Triple Purse-String Telescoped PG: A "Sutureless" Pancreatico-Enteric Anastomosis

The preliminary steps of a PD have been reported previously [9]. As a general recommendation, in the case of a classical Whipple procedure, a limited (5–6 cm) partial gastrectomy is performed in order to easily perform a telescoped PG. Transection of the pancreatic distal stump is performed at the pancreatic neck or body depending on the tumor's location. The cut surface is checked for adequate hemostasis by multiple polypropylene sutures. The Wirsung's duct is left opened by putting several stiches that fix the Wirsung's mucosa to the pancreatic parenchyma. The pancreatic edge is then transfixed at its cranial and caudal edge with two 3/0 polypropylene stiches. A crucial step for performing a safe telescoped PG is to achieve adequate mobilization of the pancreatic neck and body over the arterial and venous splenic axis. The pancreatic body should be separated from the splenic vessels right to the left over a 5 cm length (Fig. 14.1). Small branches of the splenic artery and vein are selectively controlled by suture ligation with 6/0 polypropylene stiches. Generally the dissection is pursued until one reaches the groove impressed by the splenic artery on the pancreatic body. This point generally marks a reduction in the diameter of the pancreatic body. At that point a transversal incision is made on the posterior wall of the stomach at 5–7 cm from the transection line. The diameter of the gastric incision is calibrated to be 1 cm less than the transversal diameter of the pancreatic stump. A first concentric mucosal purse-string suture of Monocryl 4/0 is applied followed by two seromuscular purse-string sutures of 3/0 Monocryl in concentric fashion around the posterior gastric incision (Figs. 14.2, 14.3, and 14.4). The mucosal purse-string suture is passed into the gastric cavity, either by the open distal gastric stump or by an anterior gastrostomy in case of pylorus-preserving PD. Then, the pancreatic remnant is invaginated into the gastric cavity through the posterior gastrostomy by progressive traction on the two stay sutures (Fig. 14.5). Ideally the pancreatic remnant should protrude into the gastric cavity around 3 cm, and invagination should be pursued until reaching the point where the pancreatic body changes in its diameter (splenic groove). The two concentric seromuscular purse-string sutures are tightened

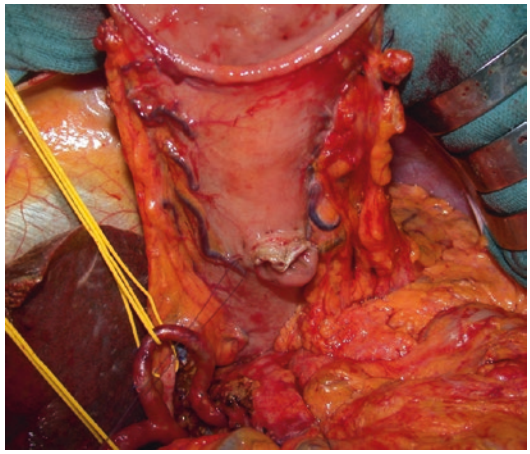

Fig. 14.2 Intraoperative view of fashioning the triple purse-string telescoped PG. The first seromuscular purse-string suture has been applied

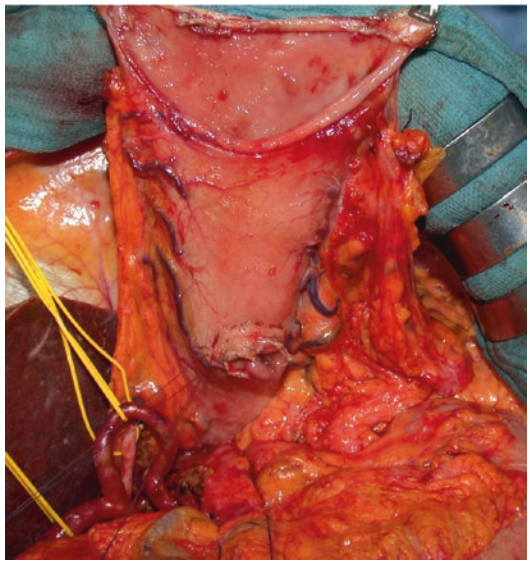

Fig. 14.3 Intraoperative view of fashioning the triple purse-string telescoped PG. The second seromuscular purse-string suture has been applied

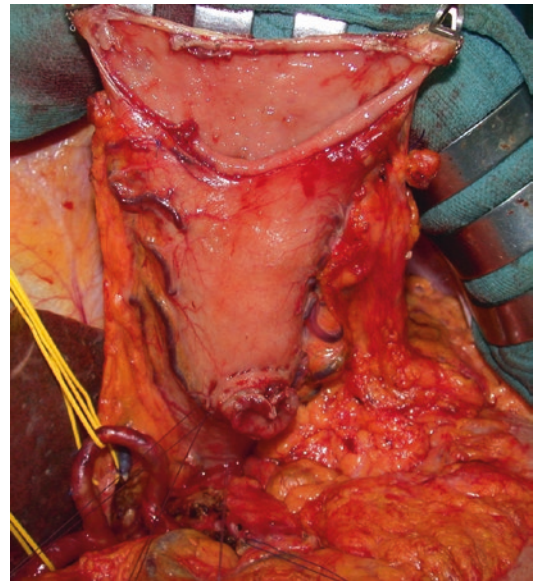

Fig. 14.4 Intraoperative view of fashioning the triple purse-string telescoped PG. The mucosal purse-string suture has been applied

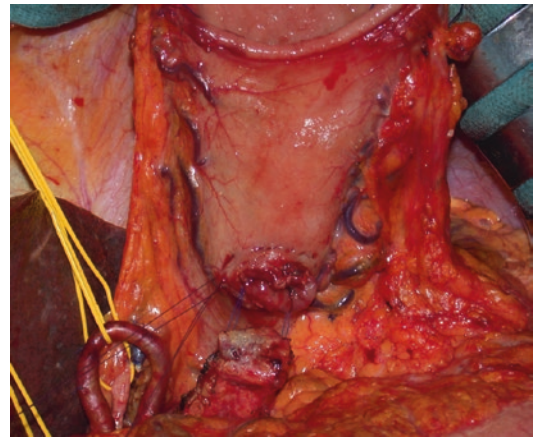

Fig. 14.5 Invagination of the pancreatic stump into the gastric cavity

with minimal tension in order to avoid pancreatic duct occlusion and postoperative pancreatitis (Fig. 14.6). Through the gastric stump, the mucosal purse-string suture is tightened over the invaginated pancreatic stump (Fig. 14.7). This last suture guarantees appropriate hemostasis of the gastric mucosa. In all cases an omentoplasty is performed around the PG. Two abdominal drains should be placed close the PG through the foramen of Winslow (right drain) and the lesser sac (left drain). The drains are removed at the fifth postoperative day in the absence of pancreatic fistula (Fig. 14.8).

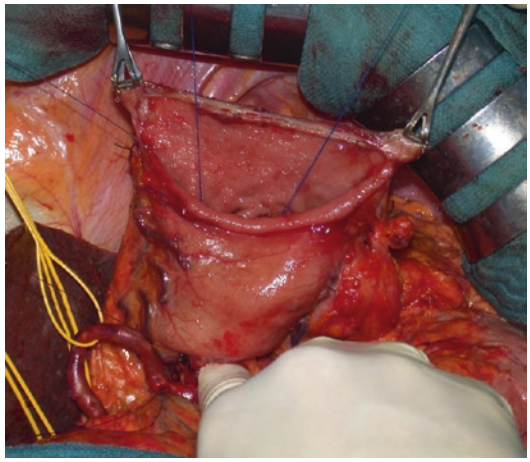

Fig. 14.6 Tightening of the two seromuscular purse-string sutures

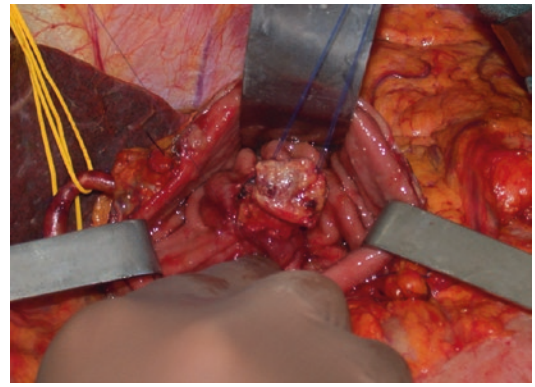

Fig. 14.7 Tightening of the mucosal purse-string suture

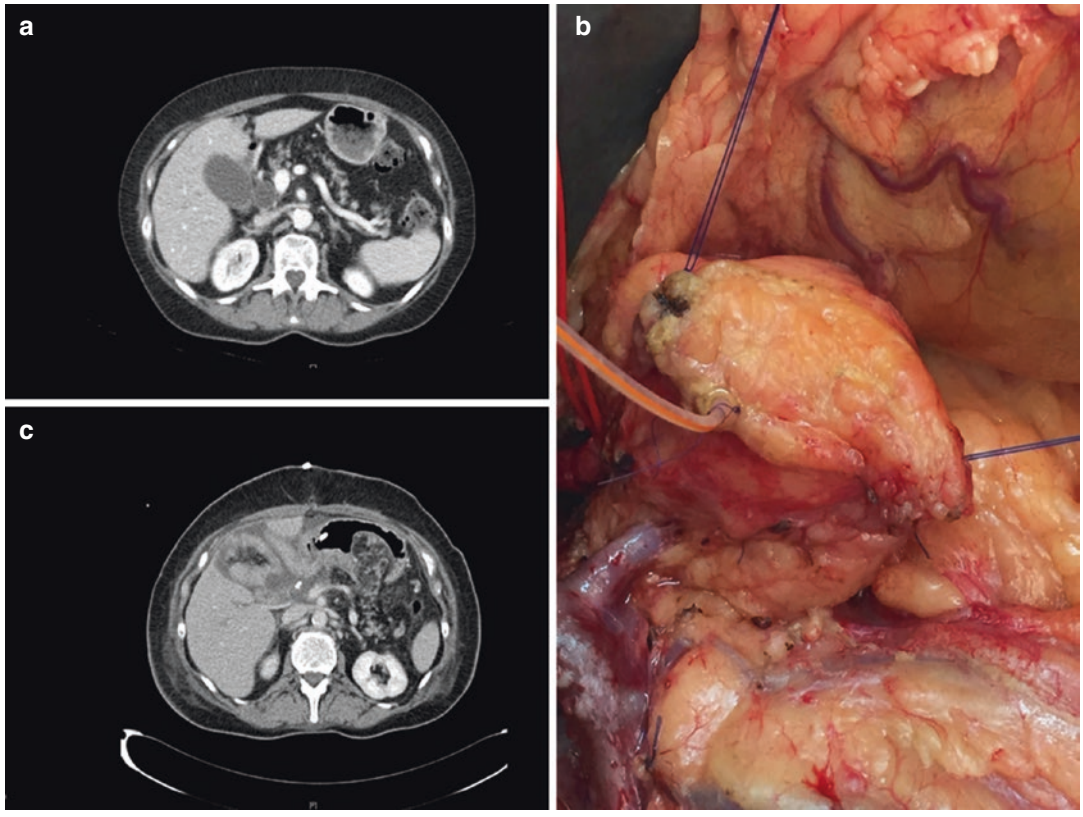

Fig. 14.8 Clinical scenario of a patient with massive fatty infiltration of the pancreas who underwent PD with the triple purse-string technique. A 5 french stent is in place juste to show the diameter of the Wirsung, however stent are never used with this technique. (**a**) Preoperative CT scan showing a diffuse fatty infiltration of the pancreas; (**b**) intraoperative picture of a fatty infiltration of the pancreas; (**c**) abdominal CT scan at postoperative day 10 showing the normal appearance of the PG with the invaginated pancreatic remnant

14.3 Postoperative Care and Management of Complications

All patients should have a gastric decompression by a NG tube until postoperative day 5, at that time NG is removed and oral intake is progressively introduced. At postoperative day 7, all patients should have a CT scan examination of the abdomen in order to detect any form of abdominal complications early. The most frequent complication of this type of anastomosis remains the upper GI bleeding that is seldom a consequence of inappropriate pancreatic stump hemostasis and appears in the 2 first postoperative days. Late GI bleeding is rather the consequence of pancreatic stump erosion by pancreatitis. This kind of bleeding is frequently massive and sudden and can be associated with inhalation pneumonia and hemorrhagic shock. A prompt endoscopic and/or surgical treatment should be carried out. The compliance of the gastric cavity can accommodate a great quantity of the blood and clots; very rarely conservative measures can manage this type of bleeding. Delay in prompt management of this type of complications is a source of mortality. When endoscopic treatment is not feasible or not available, laparotomy with direct hemostasis of the pancreatic stump by an anterior gastrostomy easily manages this type of complication.

Conclusions

We describe an easy, reproducible, and safe technique used to perform an invaginated PG which minimizes the rate of PF after PD. The basic principles of this technique are based on the large mobilization of the pancreatic stump over the splenic vessels, the adequate invagination of the pancreatic remnant into the gastric cavity, and the absence of transfixing stiches with only purse-string sutures. Because of its easiness of creation and reproducibility, this technique should be compared in a prospective trial with conventional PJ techniques.

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Portal Vein Resection: How I Do It

15

Alexis Ulrich, Pietro Contin, and Thilo Hackert

Venous tumor infiltration of the portal vein (PV) or superior mesenteric vein (SMV) by pancreatic ductal adenocarcinomas (PDAC)—although classified as a borderline resectable finding—is not a contraindication for curative resection. This practice is widely accepted, looking at the guidelines of the International Study Group on Pancreatic Surgery (ISGPS) [1], which is mainly influenced by the recommendations of the National Comprehensive Cancer Network (NCCN) [2] However, venous infiltration can cause irresectability when the remaining diameter of the vein—mostly at the site of the superior mesenteric vein (SMV)—is too small to ensure adequate drainage of the blood from the small bowel to the liver. A good impression of the resectability can be achieved by preoperative contrast-enhanced computed tomography (CE-CT). Characteristic findings of venous infiltration are a reduced diameter or occlusion of the PV or SMV lumen as well as the extension of contact between the tumor and the vein circumference of >180°. In the majority of cases, the necessity for venous resection can be expected and planned preoperatively by evaluation of the CE-CT.

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Several factors have to be considered before attempting a venous resection.

1. Are the diameters of the remaining cut ends of the vein—after resection—appropriate for anastomosis, allowing blood flow from the small bowel to the liver?
2. Can the splenic vein (SV) be preserved?
3. Is there a need for interposition of an allograft/patch, or can an end-to-end anastomosis without interposition be performed?
4. Which allograft/patch—if required—is the most appropriate one in the individual situation?

The most common limitation for SMV/PV resection occurs in cases where the tumor invades the mesentery of the small bowel which may lead to technical irresectability, as the remaining SMV or its branches would be too small for a technically and functionally safe anastomosis.

During the operation, it is of paramount importance to be prepared for resection as the time of vein clamping should be as short as possible. During the clamping time, venous congestion of the small bowel can occur, impairing the healing of the latter anastomoses (pancreaticojejunostomy, hepatico-jejunostomy, and gastrojejunostomy). In doubt, simultaneous clamping of the superior mesenteric artery (SMA) might be an option to avoid excessive congestion and subsequent bowel edema after reperfusion.

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The SV is involved in the tumorigenic infiltration on the level of the venous confluence in many cases, requiring its partial resection. Due to collaterals, the SV not necessarily has to be reinserted into the PV in most patients. However, in case of venous congestion of the spleen, a splenectomy or reinsertion of the SV into the PV is of benefit. The reinsertion, however, should not create too much lateral tension on the PV/SMV anastomosis as this could lead to a narrowing of the vessel lumen with a higher risk of postoperative thrombosis. Attention should also be given to the gastric coronary vein (CV), which might be the only venous drainage of the stomach, if the SV has to be resected, most commonly in patients who undergo total pancreatoduodenectomy combined with splenectomy. Anatomically, the CV can drain into the SV or the PV which should be clarified intraoperatively to evaluate the possibility of CV preservation or of reinsertion, if necessary.

For restoration of continuity of the PV/SMV axis, in the majority of cases, no interposition is required to bridge the defect after PV/SMV resection, and an end-to-end-anastomosis is feasible. However, tension should be avoided as it increases the risk of thrombosis. Therefore, the right hemicolon and the mesenteric root of the small bowel should be completely dissected from the retroperitoneum, the lateral side wall, and the major vessels (aorta, vena cava, Cattell-Braasch maneuver). This creates the necessary flexibility to lift the small bowel together with the mesentery root toward the upper abdomen.

If the distance remains to be too long for a direct anastomosis, a graft interposition has to be used. Various options are available and are discussed later. If possible, autologous material should be chosen, as the risk of thrombosis and infection is reduced compared to synthetic materials.

According to the ISGPS guidelines, four types of resection and reconstruction are used [1].

In case of only short segmental attachment of the tumor to the vein, a tangential resection might be oncologically sufficient. The vein can be clamped with a Satinsky (or any other vascular) clamp and the tumor be resected. Afterwards, the vein integrity is reconstructed by running a suture with, e.g., 5-0 polypropylene threads (type 1 reconstruction) (Figs. 15.1 and 15.2). Attention has to be put on the

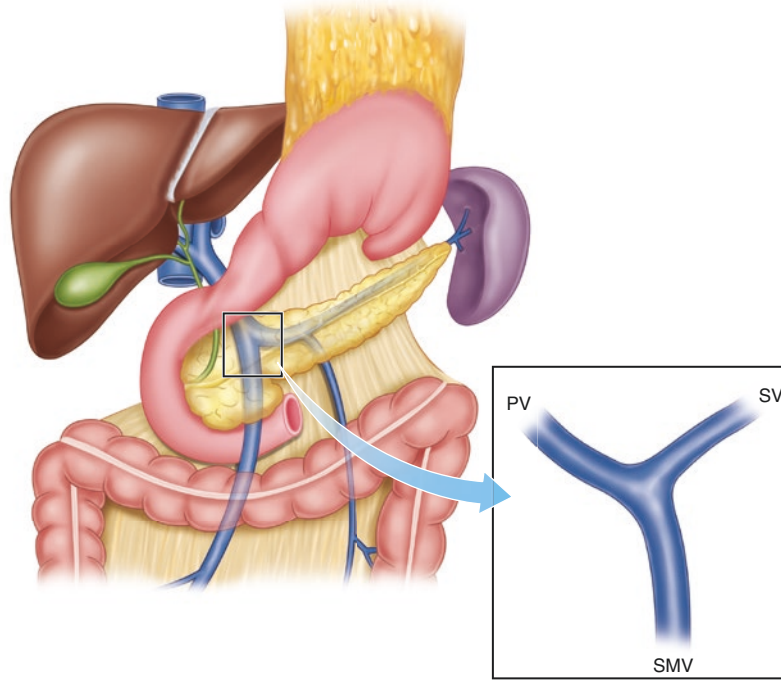

Fig. 15.1 Anatomy of the right upper abdominal quadrant with accentuation of portal (PV), splenic (SV), and superior mesenteric vein (SMV)

diameter of the vein, as this type of reconstruction could lead to a stenosis of the vein, impairing the drainage of the venous blood from the small bowel. To avoid this narrowing, the longitudinal venous defect may be closed transversally (Fig. 15.3), according to the technique known for pyloroplasty. This closure is appropriate for defects up to 2 cm in length and preservation of at least half of the circumference. The possibility for this type of closure, however, may be limited by the possibility of venous kinking that can occur. An alternative in this situation would be the closure of the defect with a patch (type 2) (Fig. 15.4). Besides bovine or artificial patches, autologous material is suitable for patch creation. Autologous venous patches can be taken from the left renal vein (close to the vena cava under preservation of the respective ovarian/testicular vein to ensure preservation of venous renal drainage), from the cava itself, or from the jugular vein. A recent publication suggested the creation of the patch from the parietal peritoneum [3]. A part of the peritoneum is harvested from the lateral abdominal wall together with the dorsal fascia of the rectus muscle. The patch is placed onto the PV/SMV defect with the peritoneal side positioned toward the lumen and fixed by running sutures (i.e., polypropylene 5-0).

Frequently, a part of the PV/SMV is completely obstructed by the tumor, and a complete segment has to be resected. In the majority of cases, a direct anastomosis of the both ends of the vein is feasible (type 3). As mentioned above, the root of the small bowel and the right hemicolon should be mobilized for more flexibility. If possible, the SV should be preserved, if necessary, by a diagonal cut of the PV/SMV even if the

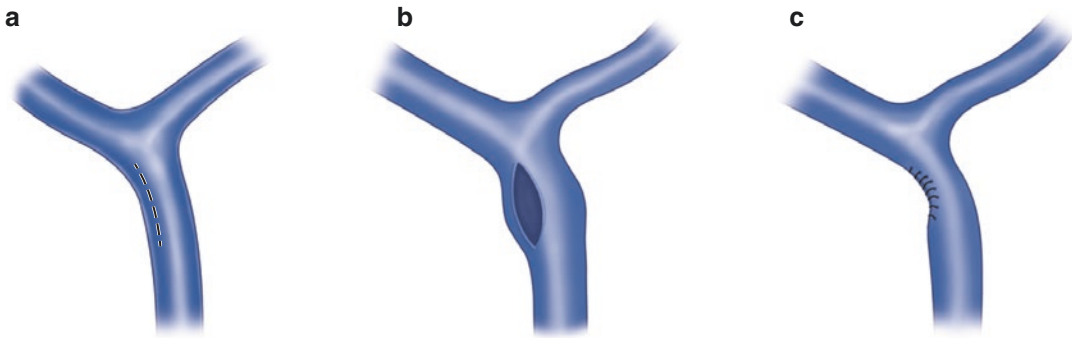

Fig. 15.2 Partial resection of the SMV (**a**), appearance of the defect (**b**), and closure of defect by running suture (**c**) without interposition (type 1 resection according to ISGPS)

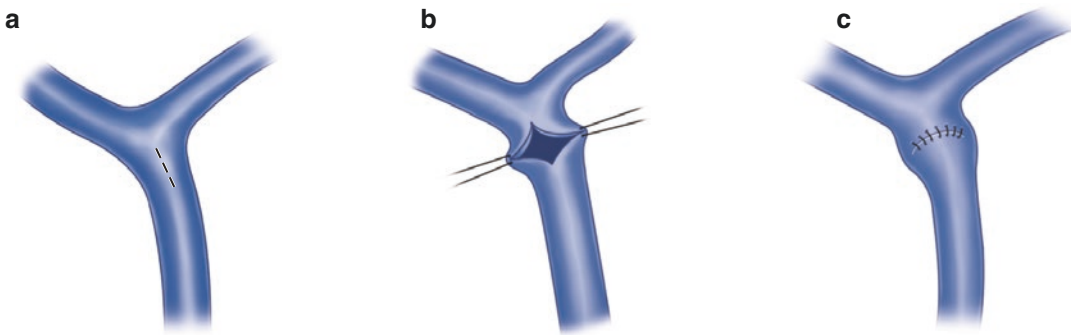

Fig. 15.3 Partial resection of SMV (**a**), lateralization of the side walls of the defect (**b**), and closure of the venous defect transversally (**c**)

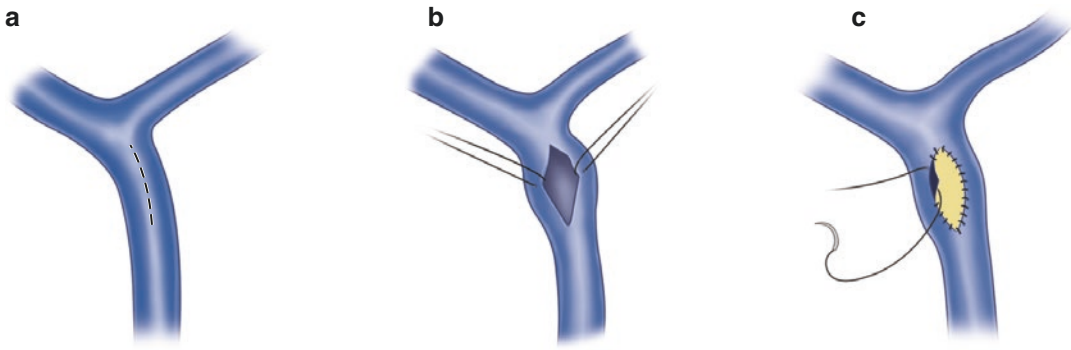

Fig. 15.4 Partial resection of SMV (**a**), appearance of the defect (**b**), and closure of the venous defect by insertion of a patch (**c**) (type 2 resection according to ISGPS))

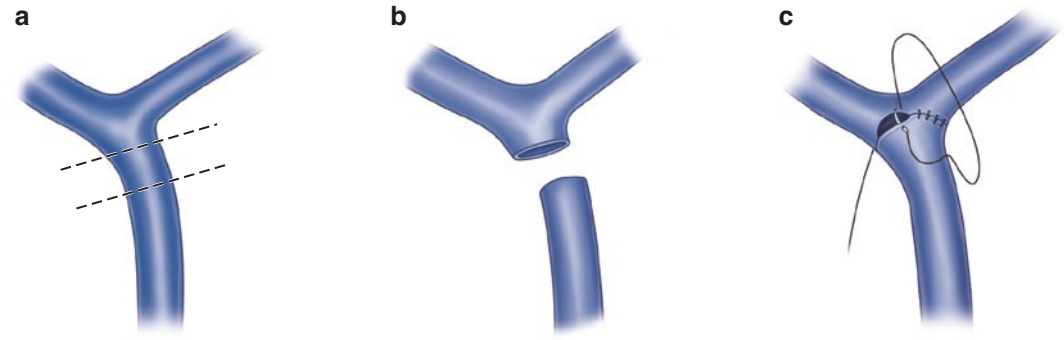

Fig. 15.5 Segmental resection of the SMV (**a**) with a defect that has to be bridged (**b**) and closure by end-to-end anastomosis (**c**) (type 3 resection according to ISGPS)

diameter of the PV end exceeds the diameter of the SMV end by factor of 2 or 3. The vessels can be clamped with vascular clamps of each kind. However, it has to be resected so that both vein ends are not twisted. If large distances have to be bypassed, larger vascular clamps are helpful to pull the SMV together with the mobilized bowel toward the upper abdomen. Afterwards the two cut ends are connected. We normally use a 5-0 polypropylene, double-armed, running suture, starting with the posterior wall from the median to the lateral edge. In case of fragile veins and a large distance to bridge, the first suture line should be created in a parachute technique and approximated, when the thread of the complete posterior wall is set up. The anterior wall is also sutured with a new double-armed thread starting from the lateral border to the middle of the vein. The same is done from the median edge using the remaining end of the first thread. In the middle of the vein, the both ends are tied with a loose knot of up to 1 cm, after the clamps are opened (Fig. 15.5). Thereby, a narrowing of the anastomosis can be prevented as the loose knot allows the elastic vessel wall to adapt to the increasing diameter after reperfusion. Potential minor bleedings at the suture line usually stop without further measures.

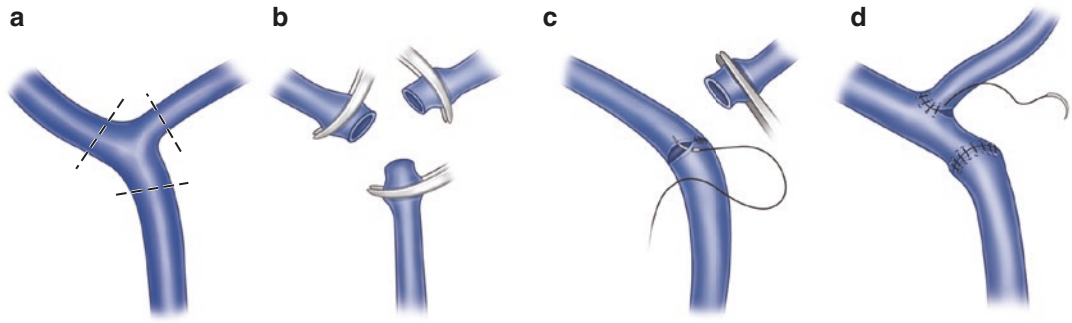

Fig. 15.6 Segmental resection of the SMV and SV (**a**) with a defect that has to be bridged (**b**), closure by end-to-end anastomosis of PV and SMV (**c**), and reinsertion of the SV into the PV (**d**)

As mentioned before, sometimes the SV cannot be preserved. If a reconnection is necessary and feasible (tension), the PV/SMV is clamped again after completion and opening of the first end-to-end anastomosis and a lateral incision of the PV/SMV are made according to the width of the SV. The posterior and anterior walls are sutured with 5-0 polypropylene running stitches (Fig. 15.6).

A type IV reconstruction with interposition of the PV/SMV has to be regarded as an absolute exception, as it is just rarely necessary. As material for interposition, the following can serve:

- Saphenous vein
- Internal jugular vein
- Left renal vein (close to the vena cava)
- External iliac vein
- Gonadal vein
- Peritoneal patch
- Bovine patch
- PTFE prosthesis

The advantage of autologous material is the reduced risk of infection; however, it is associated with more surgical efforts and should be harvested before clamping of the PV/SMV to avoid a prolonged ischemia time of small bowel and liver. If no suitable autologous vein segment is available, a tubular interposition graft can also be created from a peritoneal or bovine patch, which is placed around a suction tube or tubular instrument of the required diameter (Fig. 15.7).

The insertion technique is the same as for a direct end-to-end anastomosis with the exception that two anastomoses have to be performed (Fig. 15.8). Loose knots at the end of the anastomosis are recommended, again, if autologous material is used. In PTFE prostheses, this is not required or recommendable as the synthetic material has a fixed diameter and shows no adaptive potential.

To evaluate patency of the reconstructed PV/SMV, routine duplex ultrasound examinations are performed postoperatively, and serum liver enzymes are closely monitored to recognize potential venous flow impairments immediately. In doubtful duplex findings suggesting stenosis or occlusion of the anastomosis, a CE-CT is the diagnostic method of choice to clarify the situation and allow decision-making for the further management.

In general, no further specific anticoagulation is required after venous resection. We use low dose heparin for 6 weeks after the operation that can be stopped thereafter without ongoing anticoagulation.

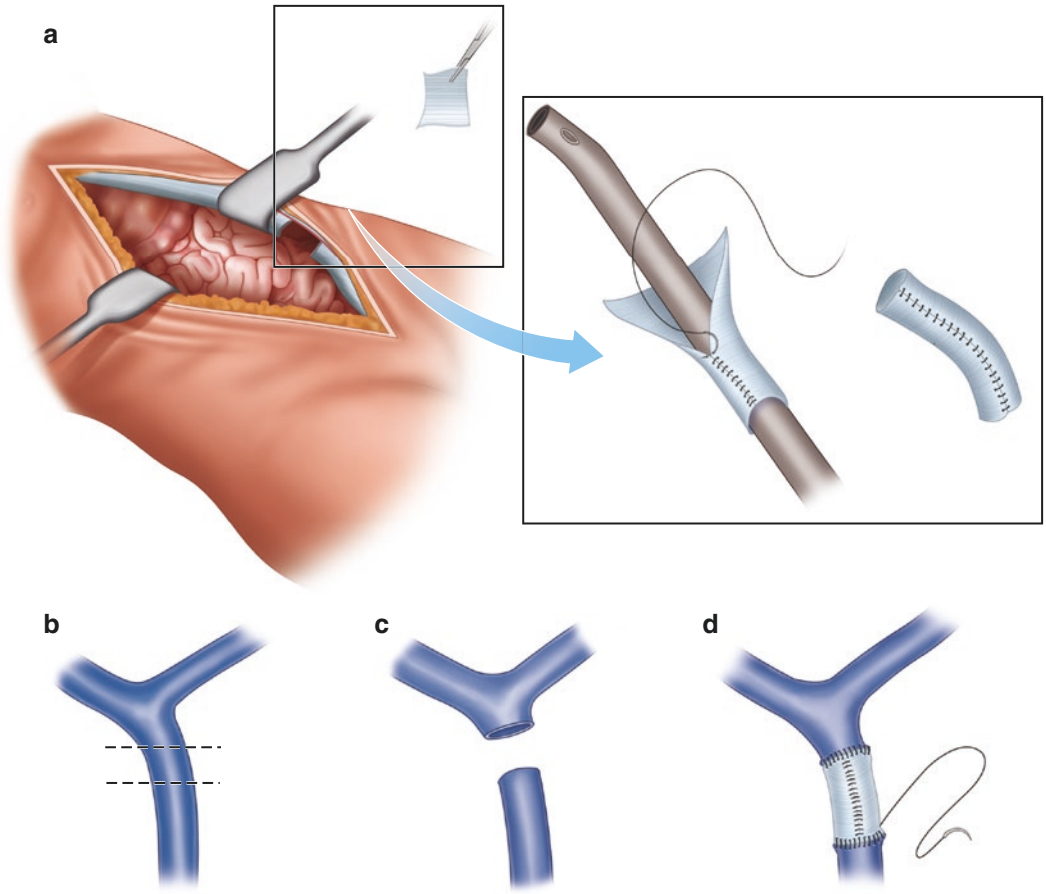

Fig. 15.7 Removal of peritoneal side wall and creation of a tubular interposition graft around a suction tube or tubular instrument (**a**). Segmental resection of the SMV (**b**) with a defect that has to be bridged (**c**) and interposition with the newly created graft (**d**)

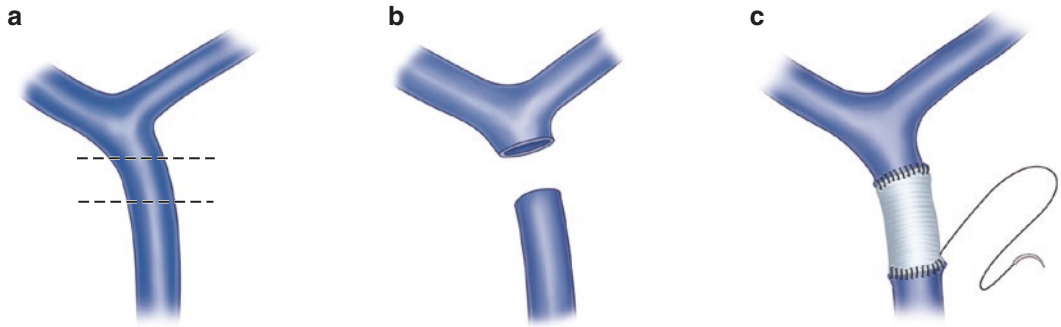

Fig. 15.8 Segmental resection of the SMV (**a**) with a defect that has to be bridged (**b**) and interposition of autologous material or a PTFE prosthesis (**c**). (Type 4 resection according to ISGPS)

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Pancreaticoduodenectomy with Venous Resection: How I Do It

16

Pietro Addeo and Philippe Bachellier

16.1 Introduction

The establishment of tertiary referral centers and the well timely management of postoperative complications have largely contributed to the reduction of postoperative mortality of pancreatic resections. These improvements combined with the advances in chemotherapy regimens have let pancreatic surgeons to the development of extensive resection in case of pancreatic tumors abutting or infiltrating the major peripancreatic vessels. In case of pancreatic adenocarcinoma, a local extension with a various degree of infiltration to the superior mesenteric and/or coeliac venous and arterial vessels is a common finding in about one-third of the newly diagnosed cases. The infiltration of the coeliac trunk and the superior mesenteric artery is classically considered as a synonymous of unresectable locally advanced disease. In such circumstances various combinations of neoadjuvant chemotherapy or radiochemotherapy regimens are used for tumor's downstaging. In these circumstances resection will be therefore considered only in some selected patients showing stable or responding disease [1]. On the contrary the infiltration of the splenomesenterico-portal (SMP) venous axis is nowadays no more considered as contraindication to a curative resection [2, 3]. The rationale behind such extensive resection is to obtain a margin-free resection without additional postoperative morbidity and mortality compared with a standard pancreatectomy. Whether patients with venous infiltration should undergo upfront resection or neoadjuvant treatment with secondary resection in case of good response to preoperative treatment remains at the moment debated [4]. It is more likely that with the advent of FOLFIRINOX® regimens which showed a higher rate of pathological response compared with previous gemcitabine-based chemotherapy, all patients presenting with resectable or locally advanced pancreatic cancer will receive preoperative chemotherapy in the near future [5]. Nevertheless the prognostic value related to the presence of a histologically proven venous invasion remains unclear because of the small size of the cohort analyzed, heterogeneity in patients' population, and the lack of information regarding the presence and/or the depth of the venous wall invasion in different comparative studies reported [4, 6]. Some authors identified venous invasion as a consequence of pure tumor localization [7], while others identified venous invasion as a poor prognostic factor [4, 6]. Other studies pointed out the importance of tumor depth infiltration into the venous wall, identifying intimal invasion as a

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poor prognostic factor [8]. In the modern era of pancreatic surgery, different single-center and multicenter studies have shown the safety of pancreatectomy with venous resection. Morbidity and mortality of pancreatectomy with venous resection are not different from those of standard resection in pair comparison [2, 4]. However there is still a lack of a standardized surgical technique described that may limit the diffusion and reproducibility of the good results reported by tertiary centers in different environments. The present chapter will describe a standardized surgical technique used to perform a "safe" pancreaticoduodenectomy with venous resection.

16.2 The "Safe" Venous Resection

The concept of safe venous resection was developed at our center during the last 20 years and refers to a technique that is devoted to minimizing intraoperative bleeding, maintaining an optimal blood flow to the liver and the bowel, and achieving an oncologic radical resection [9–12]. This surgical strategy entails the fact that venous resection should be planned before surgery or at least anticipated early in the course of a pancreatic resection, and venous resection should be performed as en bloc procedure as the last step of the resection phase (Fig. 16.1). This technical issue has several potential advantages. First, it avoids eventual manipulations on a newly constructed vascular anastomosis that can end up to its disruption in the case of venous resection performed before the detachment of the pancreatectomy specimen from the coeliomesenteric arterial axis. Second, it allows for a complete clearance of the retroportal lamina with consequent complete devascularization of the specimen and correct oncologic resection. Third, the complete clearance of the retroportal lamina from the coeliac trunk and the superior mesenteric artery allows for a correct and tension-free venous anastomosis. All attempts made in order to dissect an adherence between the SMP axis and a PD specimen should be proscribed because

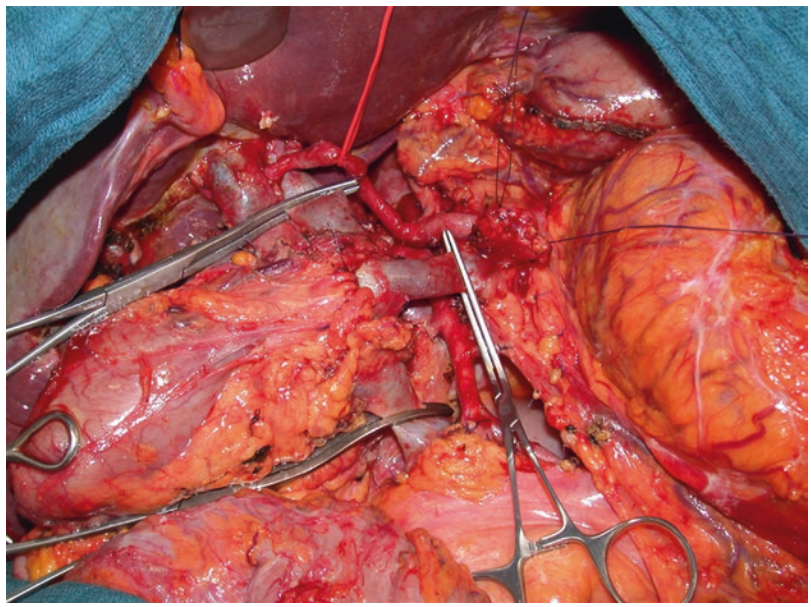

Fig. 16.1 Intraoperative view of a pancreaticoduodenectomy (PD) with resection of the SMP venous axis. The PD specimen is left attached only to the venous axis as the final step before venous resection. The SMA and the CT have been previously completely cleared of the retroportal lamina

source of a life-threatening bleeding and of tumoral seeding. At the same time, wedge resection, in our opinion, should be avoided because of their limited oncologic and technical value. Lateral venous resection can be performed in very few cases when tumoral infiltration does not encompass more than 90° of the venous axis circumference and no more than 2 cm of length. Beyond these particular conditions, a lateral venous resection carries a high risk of venous axis distortion, uncertain oncologic margins, and increased risk of thrombosis. In our experience this type of resection is therefore generally avoided, and segmental resections are routinely performed.

16.3 Planning a Safe Venous Resection

Accurate preoperative imaging by CT scan with venous phase is helpful in correctly detailing the presence and the extent of venous invasion in case of periampullary malignancy. The extension of venous invasion can be therefore classified according to Nakao et al. or Ishikawa et al. [13, 14]. However, even with the best available modern imaging, up to 40% of venous axis tumoral abutments are currently diagnosed intraoperatively [15]. Distortions of the venous axis, unilateral or bilateral abutments, are common finding which may anticipate preoperatively venous infiltration. The length and the location of the future venous resection are then planned by the tumor's location. Isolate resection of the portal vein is quite uncommon in pancreatic adenocarcinoma and more often observed in distal cholangiocarcinoma as a consequence of massive perineural infiltration. For pancreatic adenocarcinoma invasion is more frequent at the level of the SMP venous confluence as a consequence of tumor location in the medial aspect of the pancreatic head. For pancreatic adenocarcinoma located in the uncinate process, infiltration is more frequent at the level of the superior mesenteric vein up to the ileocolic and jejunal branch confluence. We use a simple classification (Fig. 16.2) that can guide the performance of a venous resection according to the type of segment invaded: Type I, tumors infiltrating the portal vein; Type II, tumors infiltrating the SMP venous confluence; Type III,

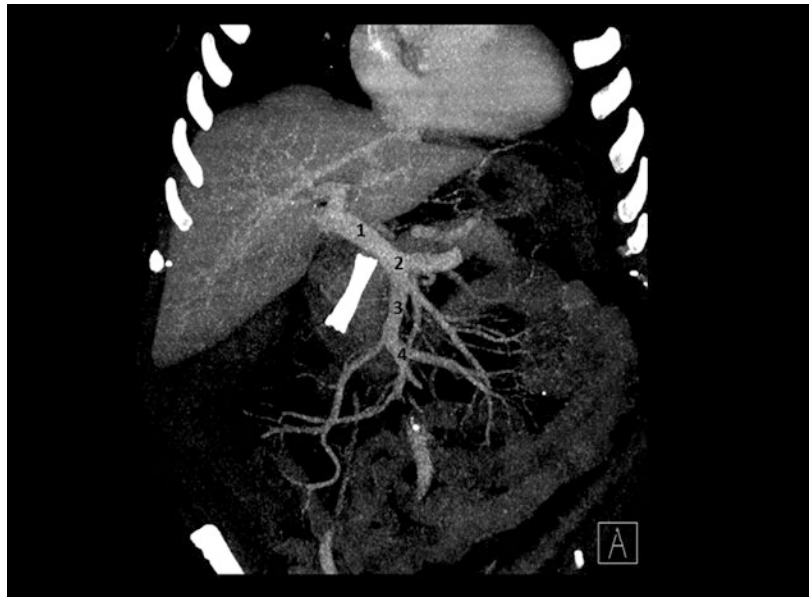

Fig. 16.2 A simple and easy-to-use classification for localization of venous resection according to the type of resected segment

tumors infiltrating the origin of the SMV vein; and Type IV, tumors infiltrating the venous branches at the origin of the SMV [16]. In some cases the extension of invasion to the venous SMP axis can be a combination of the least two types as generally seen in case of locally advanced tumors.

16.4 Common Surgical Steps

Some authors have raised questions about the maximal length of venous segment that can be safely resected during a pancreatectomy [17]. It is more likely that in a common Whipple's procedure, such as originally described, the resection of even 2 cm of the portal vein appears as difficult to be achieved without tension and potential difficulties. For these reasons most of these authors describe and prefer lateral resections of the SMV axis and/or in case of segmental resection the use of graft replacement of the resected segment [4]. In our experience there are no limits in the maximal length of the venous axis to be resected, and graft replacement is not needed in case of pancreaticoduodenectomy or total pancreatectomy when some basic surgical maneuvers are performed.

First, the entire right colon and the insertion of the mesentery are taken down up to Treitz ligament (Cattel-Braasch maneuver). This maneuver allows for an easy and safe lifting of the entire bowel that will facilitate greatly the venous reconstruction. In order to approximate in a better way, the two venous ends to be anatomized in further length can be gained by mobilizing the right liver. However the same effect can be also obtained just by putting some gauze between the segment 8 and the diaphragm. One key point in order to avoid problems of venous approximation without tension is to completely clear the lymphatic tissues by performing an extensive lymphadenectomy. In our experience the lymph node clearance removes all the lymphatic tissues around the hepatic pedicle and the common hepatic artery and around the coeliac trunk and the superior mesenteric artery. In the particular case of tumors located in the uncinate process, the isolation of the superior mesenteric vein is performed low in the mesentery. This dissection begins below the transverse mesocolon that is sectioned far from the anastomotic arcades and left attached to the future specimen (Fig. 16.3). The middle colic and the right superior colic veins as well as the gastrocolic venous trunk of Henle are systematically sectioned in case of resection of the SMP confluence or of the SMV. The middle colic artery is generally sectioned as well, and its section is well tolerated and allows for a good lifting of the entire mesentery toward the liver. A final technical note is directed toward the splenic vein. The optimal surgical management of the splenic vein, in case of segmental resection of the SMP confluence, remains debated (see below). Nevertheless, when the splenic vein is sectioned and not implanted into a SMP neoconfluence, the section of this vessel by itself allows for a good lifting of the SMV toward the portal vein that avoids the use of venous graft [16].

16.5 Abdominal Exploration and Preliminary Steps

Adequate exposure of the operative field is crucial in order to perform a safe radical PD with venous resection. We prefer a bilateral subcostal incision with midline extension. This kind of incision, with an autostatic retractor, provides excellent exposure of the operative field. The abdominal cavity is carefully explored to rule out previously undiagnosed peritoneal carcinomatosis or small subcapsular liver metastasis. A Cattle-Braasch maneuver is first performed and followed by an extensive Kocher maneuver up to the left border of the aorta. Dissecting the greater omentum from the transverse mesocolon enters the lesser sac. The superior mesenteric artery (SMA) is isolated and dissected at its origin just

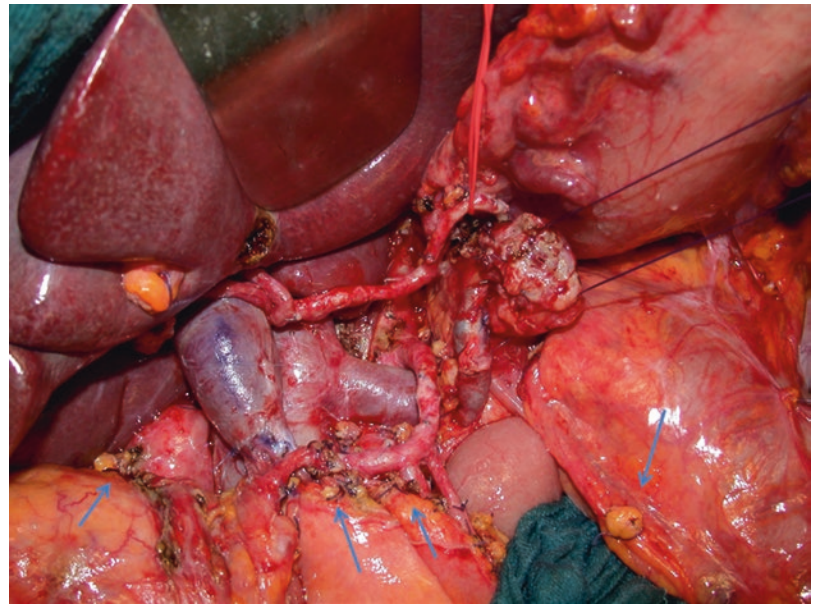

Fig. 16.3 Intraoperative view of the final aspect of a PD with resection of the SMP confluence. Blue arrows indicate the complete section of the transverse mesocolon and the low section of the mesenteric root. The marginal arcades of the colon have been respected, while the middle colic artery has been sectioned at its origin; the vascularization of the transverse colon is optimal

above the left renal vein. The first 5 cm of the SMA is easily accessed and dissected by this approach. Lymph node sampling in the inter-aortico-caval area below the left renal vein is performed and sent for frozen section. Next the dissection of the plane between the pancreatic neck and the SMV venous axis is performed. At this moment, the decision to proceed with a venous resection will be made. However, this is classically the case of a small venous involvement localized on the lateral wall of the SMP axis (Type II). In these cases the classical tunnel behind the pancreatic neck can be easily made without any risk. On the contrary when venous involvement reaches the anterior face of the SMP confluence, the origin of the portal vein, or the SMV, this step will not be technically possible (Fig. 16.1). In these cases the creation of a retro-pancreatic tunnel will be performed on the pancreatic body and delayed until the entire retroportal lamina is sectioned. This approach known also as the Whipple at the splenic artery (WATSA) has been fully described by Strasberg et al. [18]. Moreover when venous involvement is detected at the level of the SMV, the dissection will begin, as detailed above, below the transverse mesocolon. The MCV, RSCV, and the middle colic artery will be sectioned into the mesocolon while respecting the anastomotic arcades that run close to the colonic wall.

16.6 Lymphadenectomy

The procedure will start with the lymphadenectomy that will remove the lymphatic tissues and nodes along the hepatic pedicle, the common hepatic artery, and the right side of the coeliac trunk and circumferentially on the SMA. The procedure starts with a cholecystectomy. The common hepatic duct will be isolated and charged on a tape below its confluence with the cystic duct. The pedicular posteroinferior and retropancreatic lymph nodes are isolated and dissected on the right border of the hepatic pedicle. The right branch of the hepatic artery is isolated and taped. Dissection proceeds along the anterior face of the hepatic pedicle, the left

branch of the hepatic artery is dissected and taped, and the right gastric artery is ligated at its origin on the proper hepatic artery. The origin of the proper hepatic artery is isolated. Lymph node clearance proceeds on the left side of the hepatic pedicle by removing all the lymphatic tissues between the posterior aspect of the proper hepatic artery and the anterior aspect of the portal vein. At the end of the CBD, the portal vein and the proper hepatic artery, along with its right and left branches, have been isolated and completely freed. Next, the common hepatic artery in front of the upper border of the pancreas is also freed, and the lymphadenectomy is pushed until the origin of the splenic artery. The dissection plane changes and follows the celiac trunk to reach the anterior surface of the abdominal aorta to the right of the diaphragmatic crura. Care should be taken to identify a median arcuate ligament that by this lateral approach can be easily sectioned. Once the anterior surface of the CT and its right border are cleaned, the dissection will move to the SMA. The GDA is generally sectioned at this time of the operation and the stomach sectioned by gastrointestinal stapler. In case of type I tumors, isolation of the SMV is generally performed above the transverse mesocolon. However, in case of type 2, 3, and 4 tumors, the isolation of the SMV will be performed below the transverse mesocolon after having sectioned the MCV, RSCV, and the middle colic artery. Once isolated the SMV is taped. Further dissection is performed to the left of the superior mesenteric vein, removing lymph nodes from the origin of the mesenteric root. The SMA trunk is isolated to the left of the SMV low into the mesentery. The dissection will follow the anterior surface of the SMA trunk; the MCA will be taped and preserved or sectioned according to the tumor's location (see above). The ligament of Treitz is sectioned between ligatures, and a mechanical stapler sections 15 cm below the ligament of Treitz the first jejunal loop. The dissection will follow the left border of the SMA up to its origin on the aorta. The first jejunal arterial branch will be sectioned on the left border of the SMA. The SMA trunk is taped and a gentle traction is put toward the left side; by this approach the dissection will completely clear the right border of the SMA with ligation of the inferior pancreaticoduodenal arteries. The dissection, by this mesenteric left approach, will provide optimal exposure on the inferior and posterior pancreatic veins and the first jejunal venous branches that will be ligated and sectioned as well. At that time the future specimen will remain attached only on the SMP venous axis.

16.7 Preparation for a Safe Mesentericoportal Vein Resection

At this point of the operation, attention is directed toward the pancreatic body. Differently from a classical Whipple, the section of the pancreas will not be performed on the neck in order to reduce the possibilities of tumor breakout and venous injuries. We prefer to section the pancreas on the body at the distance from the neck that is dictated by the tumor location. In case of type 2, 3, and 4 tumors, the section is performed on the superior part of the body on the origin of the splenic artery or by an inferior approach which is quite easier in our opinion. The inferior border of the transverse mesocolon is sectioned far from tumoral attachments, a retropancreatic tunnel is created, and the pancreatic body is taped and lifted. This maneuver ensures optimal control of the splenic vein in case of injury. Then the pancreatic body is dissected progressively from the splenic vein, and both are separately taped. During the separation of the SV from the pancreas, care should be taken in order to avoid injuries to the small venous branches draining the pancreatic body into the SV. These are easily sectioned and sutured, especially, if this dissection has been done far from the area of tumor

infiltration. Once the SV has been taped, the pancreatic body is sectioned, and a frozen section is sent for analysis. The CBD is sectioned just below the hilar plate. At that point according to the type of tumors (see above), the dissection will proceed differently.

16.8 Venous Resection

When an isolated resection of the portal vein is planned, which is quite uncommon in case of pancreatic adenocarcinoma, the dissection is directed from the splenic vein toward the SMP confluence. The anterior surface of the SMP confluence is easily dissected, and the portal vein just below its bifurcation is taped. Next the splenic vein and the SMV will be taped. After having clamped the SMA, the SMV, the SV, and the PV, the section of a short venous segment (generally between 1 and 2 cm long) will complete the demolition phase. Reconstruction will be achieved by reimplanting the basis of the portal vein on the PV pedicular trunk by an end-to-end anastomosis.

Resection of the SMP confluence (type 2 tumors) represents by far the most frequent venous resection performed in case of pancreatic adenocarcinomas. This type of resection poses the problem of the management of the splenic vein. For this kind of resection after having sectioned the pancreas, the pancreatic body is progressively dissected from the splenic vein and artery toward the left at 4–5 cm. All venous and arterial branches will progressively be ligated by selective stiches of 5-6/0 polypropylene sutures. This is necessary in our experience for two reasons. Firstly, we exclusively perform an invaginated telescoped pancreaticogastrostomy, as a pancreaticoenteric reconstruction method. A length of 4–5 cm is necessary to achieve a tension-free anastomosis. Secondly, this dissection will provide enough length of the splenic vein in the case in which this will be reimplanted on the left renal vein (Fig. 16.4).

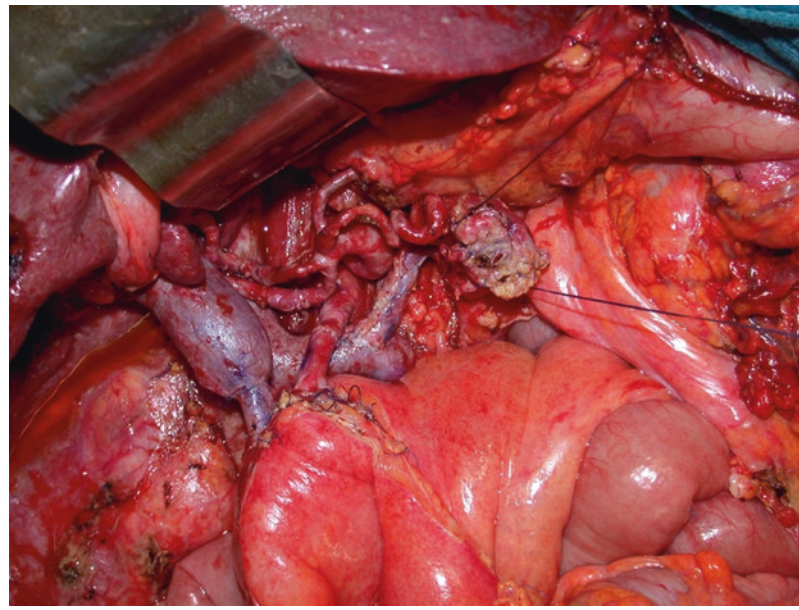

Fig. 16.4 Intraoperative view of the final aspect of a PD with resection of the SMP confluence and of the SMA. The SMV has been reimplanted on the PV, and the SV has been anastomosed in an end-to-side fashion on the left renal vein

At this point the splenic vein, the SMV, and the PV are taped. The dissection is directed toward the SMP confluence, but seldom its anterior surface is not exposed. For a segmental resection of the SMP confluence, the management of the SV will depend by several factors.

Simple ligation of the SV has been associated with the development of sinistral portal hypertension and hypersplenism on the long term. We favor all measures that can be adopted in order to avoid this phenomenon. Ligation of splenic vein without reconstruction can be performed when the natural confluence between the IMV and the SV is preserved and/or when the LGV or the MCV is preserved (Fig. 16.5). This ensures adequate venous drainage of the splenic vein into the portal system. Still secondary portal hypertension has been described using this technique [19].

The creation of an IMV-SV end-to-end anastomosis, which mimics a natural confluence, can be an alternative when the IMV drains directly into the SMV [10]. This can be performed by tailoring the IMV stump to the SV stump by some forms of venoplasty (Fig. 16.6).

Direct reimplantation of the SV vein stump into a newly constructed SMV-PV confluence is in our opinion feasible only when 1–2 cm of the splenic vein is resected (Fig. 16.7). However this type of venous reconstruction can lead, in our experience, to venous axis distortion and potential thrombosis. The interposition of a graft can be a solution in these conditions; the internal jugular vein or the left renal vein can be used with this aim. An easier and more physiologic method is represented by reimplantation of the SV into the left renal vein. This method presents several advantages. The left renal vein runs just below the axis of the SV, and direct reimplantation is quite straightforward. Secondly, the anterior surface of the LRV can easily accommodate the SV stump without any problem of caliber's incongruences. Thirdly this method avoids completely the development of any form of portal hypertension (Fig. 16.4).

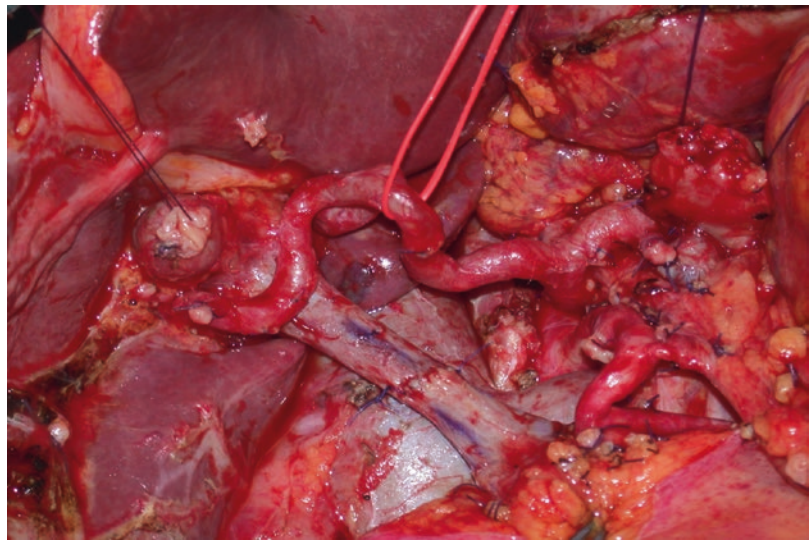

Fig. 16.5 Intraoperative view of the final aspect of a PD with resection of the SMP confluence. The SV has been ligated while preserving the natural confluence between the SV and the IMV

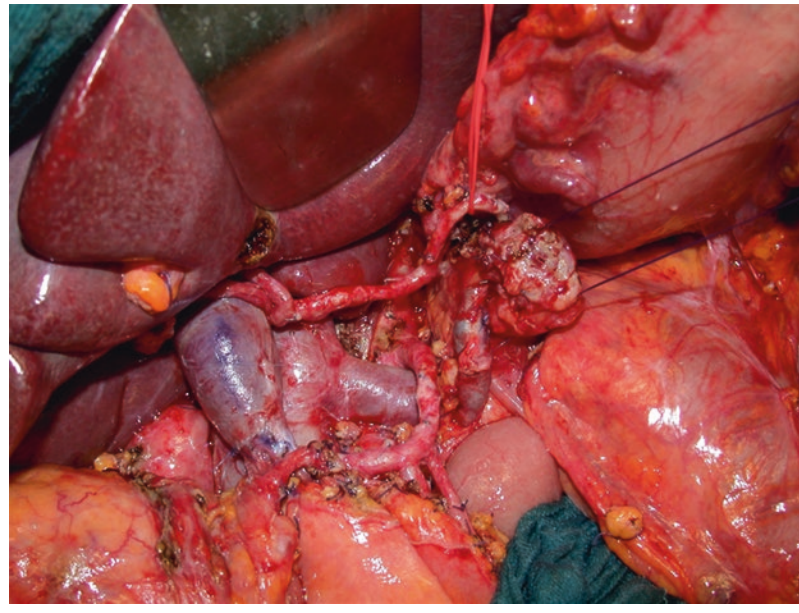

Fig. 16.6 Intraoperative view of the final aspect of a PD with resection of the SMP confluence; the SV has been anastomosed in an end-to-end fashion to the IMV

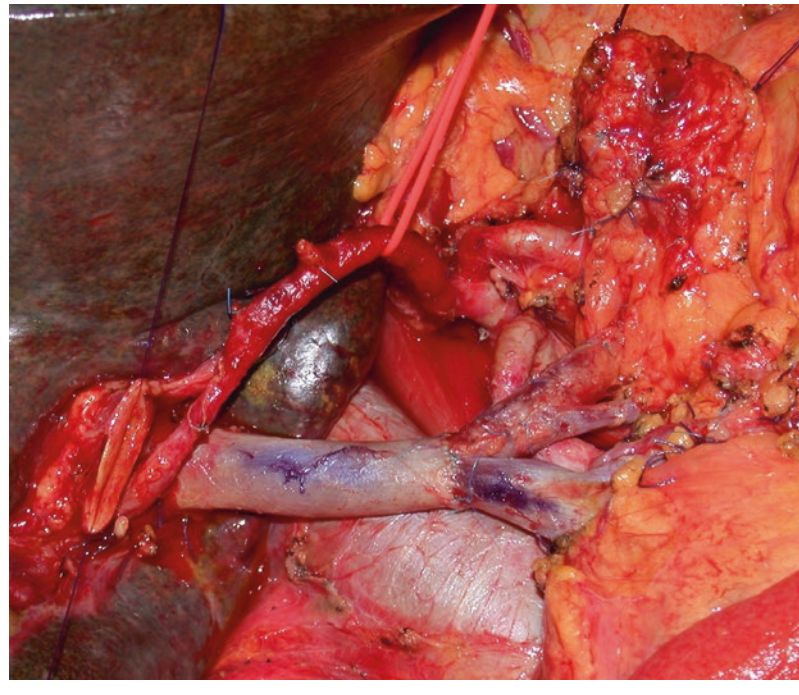

Fig. 16.7 Intraoperative view of the final aspect of a PD with resection of the SMP confluence. The SV has been anastomosed in an end-to-end fashion to the PV after having been sutured side to side to the SMV

Whatever the method chosen to manage the SV stump, the SV is at this moment sectioned. The SMA, the SMV, and the PV are clamped and sectioned, and the specimen is sent for pathology. Direct reconstruction by an end-to-end anastomosis between the SMV and the PV is fashioned by polypropylene running 6/0 sutures with a growth factor. Care should be taken in order to avoid twisting of the two ends to be anastomosed. This can be easily avoided just by marking with colors, before clamping and sectioning venous axis, the correct direction of the venous axis. This has been adopted at our unit for more than 25 years.

In case of type 3 tumors, the resected venous segment involves the origin of the SMV vein. According to the precise tumor location, the previous dissection in the mesentery has isolated either the origin of the SMV trunk or the jejunal or the ileocolic branches or both at its origin. The dissection, which follows exactly the rules described above, allows dissecting the anterior surface of the SMP venous confluence since the infiltration is seldom located on the posterior surface of the SMV by tumors of the uncinate process. At that point of the dissection, the SV, PV, SMV origin or its branches, and the SMA will be clamped. The specimen will be excised en bloc with a segment of the SMV. Reconstruction will be achieved by a direct end-to-end reconstruction with polypropylene running 6/0 sutures with a growth factor

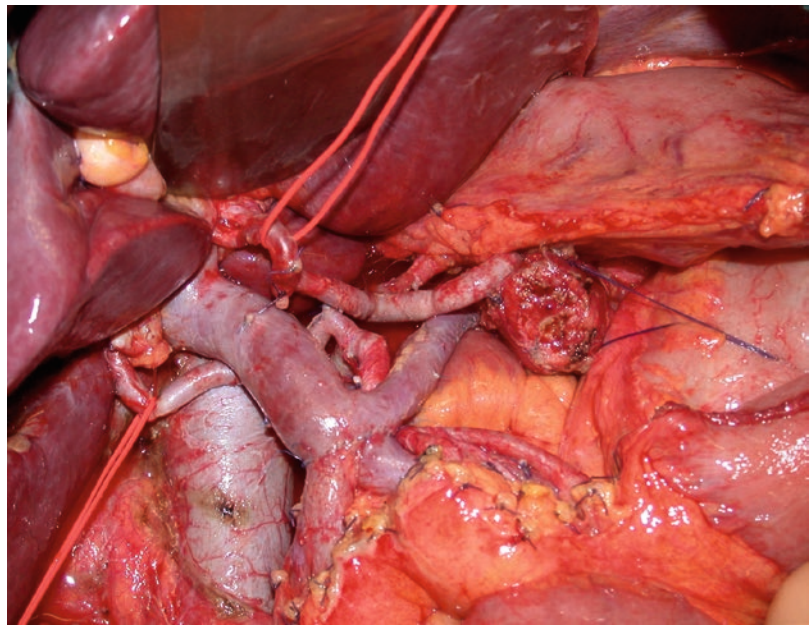

Fig. 16.8 Intraoperative view of the final aspect of a PD with resection of the SMV trunk. The origin of the SMV has been anastomosed in an end-to-end fashion to SMP venous confluence

(Fig. 16.8). When the SMV tract resected encompasses the origin of its trunk, the jejunal and the ileocolic branches will be joint together by a side-to side anastomosis on their medial aspect in a new confluence and the anastomosed in an end-to-end fashion to the basis of the SV-PV confluence.

Figures 16.9 and 16.10 depict a short intraoperative breakout of a "safe" PD with resection of the SMP venous confluence and fashioning of the venous anastomosis.

After venous anastomosis, the digestive reconstruction will follow according to surgeon's preference.

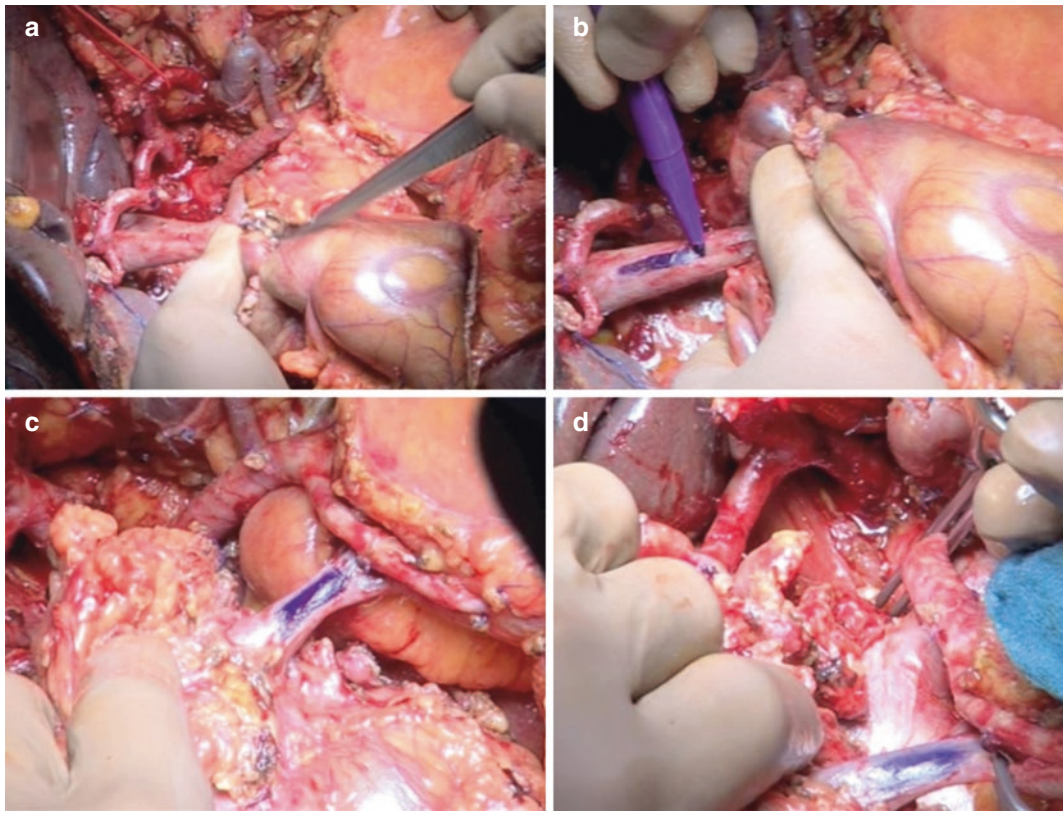

Fig. 16.9 Intraoperative view of a "safe" venous resection of the SMP confluence; (**a**) The PD specimen has been left attached to the venous axis. The splenic vein has been previously ligated and the confluence between the IMV and the SV respected. The dissection of the retroportal lamina around the CVT and the SMA is already completed; (**b**, **c**) the venous axis orientation is marked with ink in order to have correct orientation of the venous anastomosis; (**c**) The superior mesenteric artery is clamped and the venous end are transected

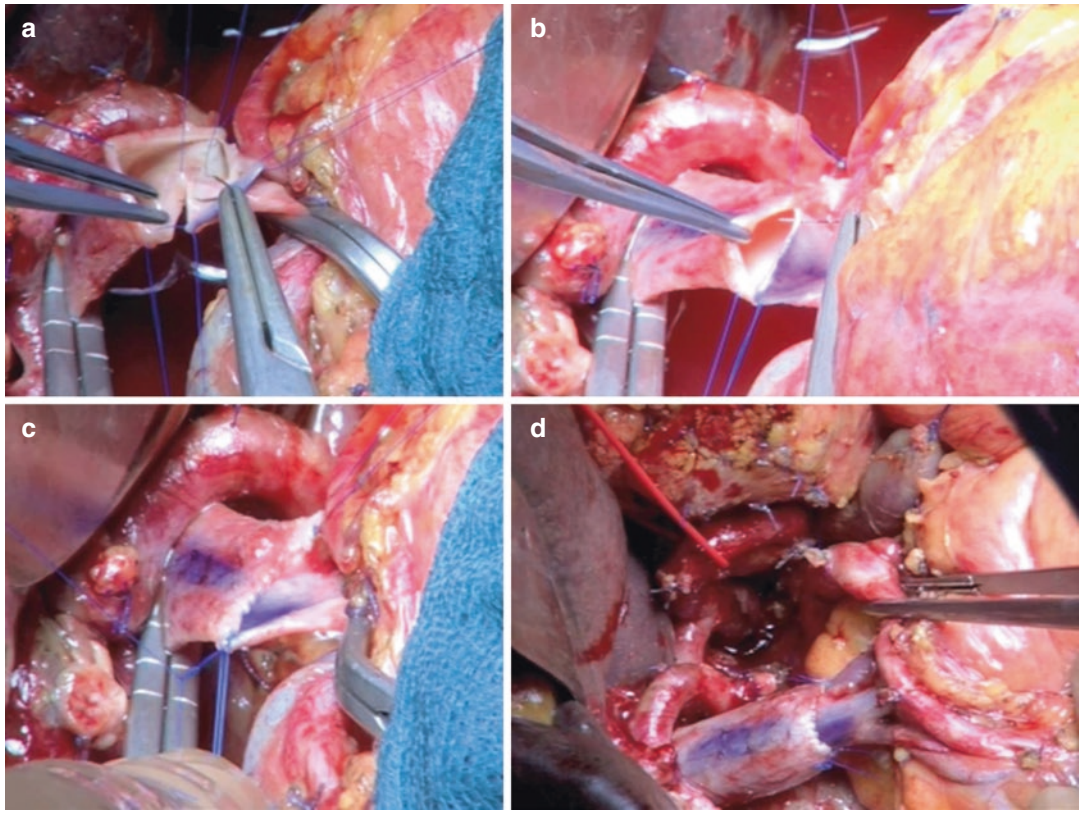

Fig. 16.10 Fashioning the venous anastomosis; The SMV and the PV are sutured in an end to end fashion. (**a**) The back wall is performed first using a 6-0 running polypropylene suture; Stays sutures are applied on the anterior wall in order to give excellent exposure of the posterior wall. (**b**) the anterior wall is performed using the same technique; (**c**) the two tunning sutures are knotted togheter with a "growth" factor. (**d**) the SMA and the venous anastomosis have been unclamped. There are no discrepancies in caliber nor in orientation

Conclusions

We describe a standardized technique used to perform a safe pancreaticoduodenectomy with venous resection, which has been used for performing more than 400 various types of pancreatectomy combined with vascular resection at our unit. The basic principles of this technique are based on the large mobilization of the mesentery, the complete clearance of the retroportal lamina around the arterial mesenteric and coeliac axis, and the optimal management of the splenic vein. These technical refinements allow the safe performance of PD with venous resection without graft interposition. PD with venous resection should be performed in high-volume HPB tertiary referral centers by surgeons with extensive experience in standard pancreatectomy and vascular reconstruction.

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17 Pancreaticoduodenectomy with the Superior Mesenteric Artery Approach: How I Do It

Takayuki Anazawa, Kyoichi Takaori, Toshihiko Masui, and Shinji Uemoto

17.1 Introduction

Previously, challenges to pancreaticoduodenectomy (PD) had arisen during the reconstruction procedure to secure the pancreatico-enteric anastomosis. Introduction of new techniques, such as duct-to-mucosa anastomosis and improved perioperative management, has improved safety, and PD became feasible. Recently, surgeons have faced other challenges, such as achievement of negative margins in case of borderline and locally advanced pancreatic cancer. After neoadjuvant chemoradiation therapies for such locally extended diseases, operative procedures became even more difficult than up-front surgery owing to adhesion, fibrotic changes, and others.

The superior mesenteric artery (SMA) is the most common site of positive margins after PD; hence, the SMA approach to PD is extremely important for early determination of the feasibility of achieving negative margins. In addition, ligation of the feeding arteries, including the inferior pancreaticoduodenal (IPDA) and gastroduodenal artery (GDA) arteries, before division of the pancreas can reduce blood loss during surgery and is a reasonable approach for performing oncologic resection. This technique has promoted the development of an "artery-first" approach. In this chapter, we introduce our techniques of "artery-first" PD with a review of the literature.

17.1.1 History of "Artery-First" PD

To our knowledge, the mesenteric approach established by Nakao et al. in the 1990s was the first to include dissection around the SMA and superior mesenteric vein (SMV) and utilize a portal vein (PV) bypass catheter as needed. It was based on the concept of "isolated pancreatectomy," which cuts blood flow of pancreatic head cancers by ligating the feeding arteries [1]. They described the "mesenteric approach" from the mesentery of the jejunum at the base of the transverse mesocolon. This approach allowed for early ligation of the IPDA and meticulous exposure and dissection along the SMA. The "mesenteric approach" evolved to the concept of the "artery-first approach," which was later proposed by Weitz et al. [2], and its international understanding becomes widespread. To date, many surgeons have advocated several methods of the "artery-first" approach to PD (Fig. 17.1) [3]. A common feature of these surgical procedures is first dissection around the SMA before committing an irreversible step in the operation. Pancreatic head carcinomas, especially those originating in the ventral pancreatic area, often

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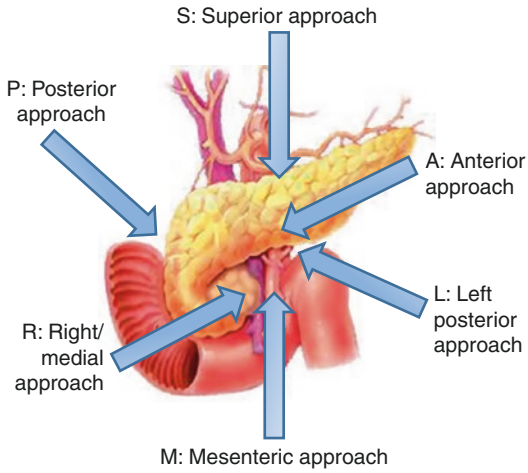

Fig. 17.1 Diagram of the six approaches to the SMA. M, mesenteric approach; S, superior approach; A, anterior approach; P, posterior approach; L, left posterior approach; R, right/medial uncinate approach; L, left posterior approach. This figure was reproduced from Reference [4]

invade from the nerve tissue around the IPDA to the periphery of the SMA. As a result, whether resection for cure or complete remission (R0 resection) is possible can be confirmed by early surgical operation, which is useful for improving the surgical indication and increasing the R0 ratio. In addition, with simultaneous GDA transection, the artery flowing into the pancreatic head becomes the transverse pancreatic artery alone, effectively reducing the amount of bleeding. Majority of general surgeons choose standard PD via the Kocher maneuver to begin mobilization. However, "artery-first" PD is performed more frequently by pancreatic surgeons.

17.1.2 Advantages of "Artery-First" PD

Advantages of "artery-first" approaches include reduction of intraoperative blood loss by blocking the arterial inflow, early judgment of arterial involvement, and achievement of negative margins along the arteries. In a case-matched study that compared "artery-first" PD (n = 21) with standard PD (n = 21), the "artery-first" PD group had significantly less intraoperative blood loss and a shorter operative time. No significant differences were found in the two groups regarding morbidity and mortality rates, overall survival, and survival according to tumor type [4]. In another series, no significant differences were found in terms of operating time, blood loss, or overall morbidity between groups undergoing "artery-first" PD (n = 40) and standard PD (n = 35). However, the "artery-first" PD group had fewer recurrences and improved survival rates than the standard PD group [5]. A recent systematic review, which included one randomized controlled trial (RCT) and 13 nonrandomized comparative studies involving 640 patients undergoing "artery-first" and 514 undergoing standard PD, concluded that "artery-first" PD was associated with better perioperative outcomes, such as blood loss, transfusion requirements, pancreatic fistula, and delayed gastric emptying. Although the overall survival rate was not superior, "artery-first" PD had lower local and metastatic recurrence rate [6]. RCTs are necessary to demonstrate the potential advantages of "artery-first" PD.

17.1.3 Demands for "Artery-First" PD

"Artery-first" PD has been advocated for over two decades by several pancreatic surgeons [3]. Recent changes in pancreatic cancer treatment have increased the demands for this method. The attempt to resect tumors with extensive local involvement has helped in the recognition of borderline resectable pancreatic cancer. Katz et al. classified borderline resectable cancer into three categories (groups A–C) based on anatomic extension and clinical features. Group A comprised patients with tumor abutment of the visceral arteries or short-segment occlusion of the SMV. Group B patients had findings suggestive but not diagnostic of metastasis. Group C patients had a marginal performance status [7]. Currently, much effort has been focused on the anatomic criteria (Katz group A), and the consensus was that operative exploration and resection may be indicated, in high-volume centers with surgical

and multidisciplinary expertise, in cases with SMV and/or PV involvement, but not in those with arterial involvement [8]. Therefore, assessing the arterial involvement at an early stage of operation became necessary, and "artery-first" PD became the operation of choice in the setting of borderline resectable pancreatic cancer.

The introduction of neoadjuvant chemotherapy and chemoradiation therapy has helped some initially unresectable pancreatic cancers become resectable. In addition, patients who underwent surgical resection after neoadjuvant therapies for locally advanced pancreatic cancer can survive as long as those with initially resectable pancreatic cancer [9]. However, the fibrotic tissue remains even after a good pathological response with a significant reduction of cancer cells; thus, predicting the pathological involvement of an artery after neoadjuvant chemoradiation therapy by diagnostic imaging alone is difficult. During surgical explorations after neoadjuvant therapies, surgeons must attempt dissection around the major arteries, such as the SMA and GDA, and determine whether to proceed with surgical resection for pancreatic cancer. In such case, "artery-first" PD is useful. Furthermore, meticulous dissection of the SMA by this approach may better achieve negative margins [10]. Accordingly, in the era of neoadjuvant therapies for locally extended pancreatic cancer, "artery-first" PD is an essential procedure.

17.2 Surgical Techniques

To perform "artery-first" PD, surgeons should be comfortable with the techniques. They are responsible for choosing appropriate techniques and should be familiar with them. Specifically, identifying the SMA in the mesentery in obese patients is difficult, and the inability to locate the SMA may hamper the safety of "artery-first" PD. We developed surgical techniques with which surgeons can easily palpate and locate the SMA even in obese patients. In our institution, we routinely use these techniques for "artery-first" PD so that surgeons in training would be able to understand the principles of the "artery-first" approach and practice it safely on their own. Our surgical techniques are presented hereafter.

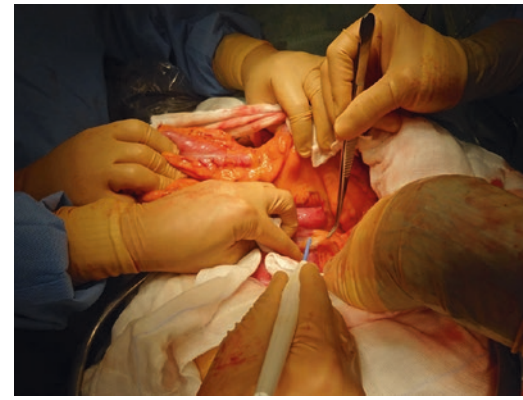

Fig. 17.2 "Tora-no-Ana" approach. The transverse colon is lifted upward, and the ligament of Treitz is divided along the lateral margin of the upper jejunum

1. "Tora-no-Ana" approach

   We use the "Tora-no-Ana" approach in pancreatic cancer cases. The term meant to indicate an opening (= Ana) through a division of the ligament of Treitz (= Tora).

   The ligament of Treitz is divided along the lateral margin of the upper jejunum, while the transverse colon is retracted upward (Fig. 17.2). The "Tora-no-Ana" is created by entering the retroperitoneal space. Then, paraaortic lymph node sampling with frozen section examination is performed. The surgeon palpates the SMA and its branches by grasping the mesentery of the upper jejunum (Fig. 17.3). In this way, regardless of how obese the patient is, the surgeon can accurately grasp the position of the SMA. During dissection, palpation may be repeated to confirm the location of the SMA. The adipose tissue of the mesentery is divided at the base of the transverse mesocolon (Fig. 17.4). The middle colic artery (MCA) may be divided at its origin for better dissection of the SMA (Fig. 17.5). The SMV and the first jejunal vein (FJV) are identified and taped to avoid incidental bleeding (Fig. 17.6).

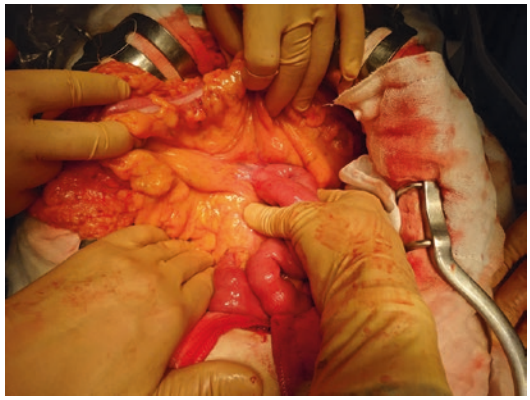

Fig. 17.3 Palpation of the SMA. The surgeon inserts his or her fingers into the "Tora-no-Ana" and palpates the SMA and its branches

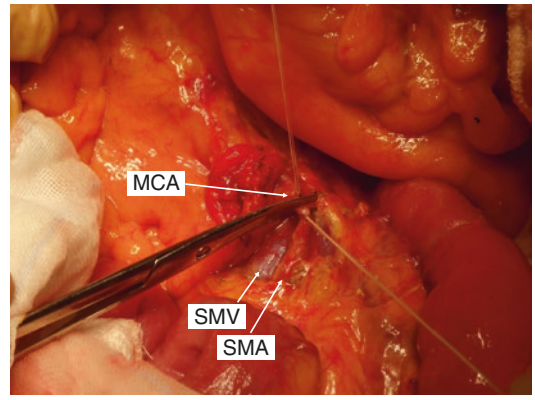

Fig. 17.5 Division of the MCA. The MCA is divided at its origin for better exposure of the SMA

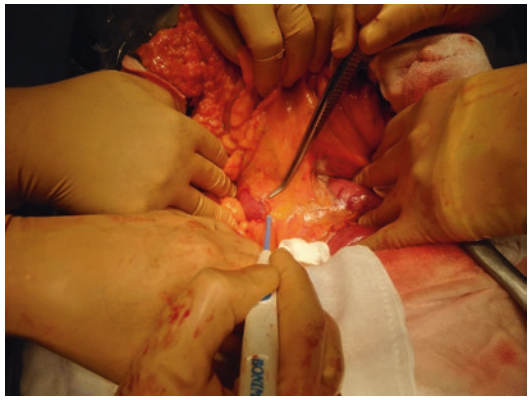

Fig. 17.4 Mesenteric approach. The peritoneum of the mesentery is divided between the inferior duodenum angle and upper jejunum

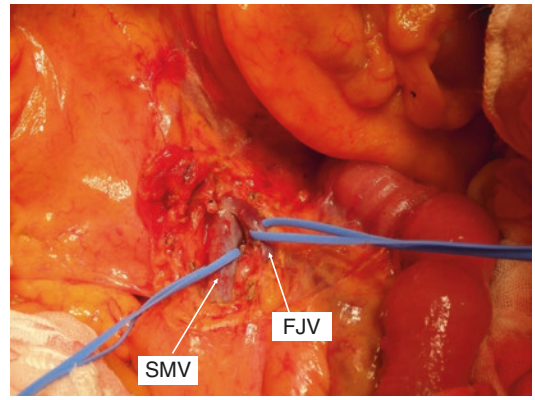

Fig. 17.6 Taping of the SMV and FJV. The SMV and FJV are exposed and taped. Avoiding incidental injury to the FJV is important

2. Division of the transverse mesocolon

   The gastrocolic ligament is divided, and the lesser sac is entered. The middle colic and right aberrant colic veins are divided. The transverse mesocolon is divided along the anterior inferior margin of the pancreatic head and body for en bloc resection of a portion of the mesentery of the transverse colon (Fig. 17.7). Moreover, preservation of the arcade of vessels along the transverse colon is mandatory to prevent ischemia of the colon.

3. Hanging maneuver of the pancreatic body

   An avascular area on the left side of the left gastric artery and superior to the splenic artery is dissected by lifting the stomach body upward, in preparation for later passage of a Penrose drain. Large Kelly forceps are inserted into the dissection plane between the pancreatic body and SMA and then advanced toward the avascular area (Fig. 17.8). The forceps are advanced without any resistance under the fusion fascia of Treitz. Advancing the forceps between the pancreatic body and splenic artery to avoid injury to the splenic vessels or dorsal pancreatic artery is not preferable. A hanging maneuver is practiced by lifting the Penrose drain passed with the large Kelly forceps, which hangs the pancreatic body and the splenic artery and vein simultaneously (Fig. 17.9). The hanging maneuver

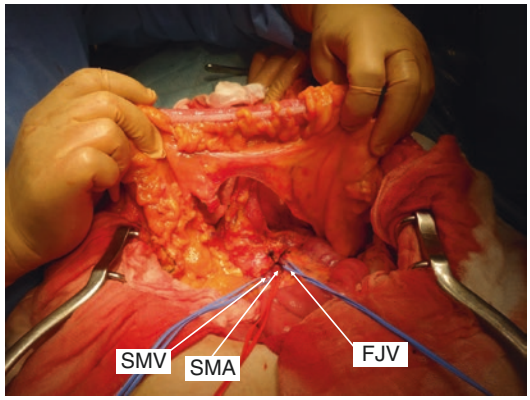

Fig. 17.7 Opening of the transverse mesocolon. The transverse mesocolon is divided along the anterior inferior margin of the pancreas

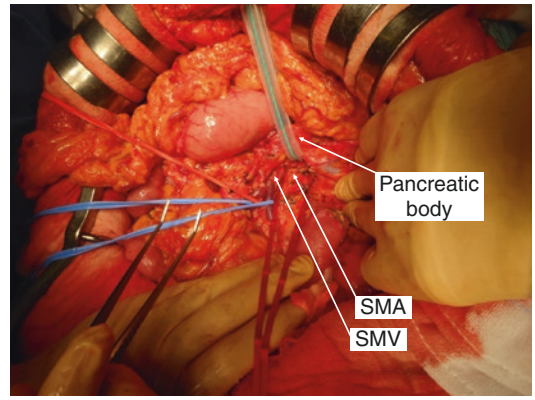

Fig. 17.9 Hanging maneuver. The pancreatic body is lifted upward by the Penrose drain. This hanging maneuver provides a better view of the proximal part of the SMA

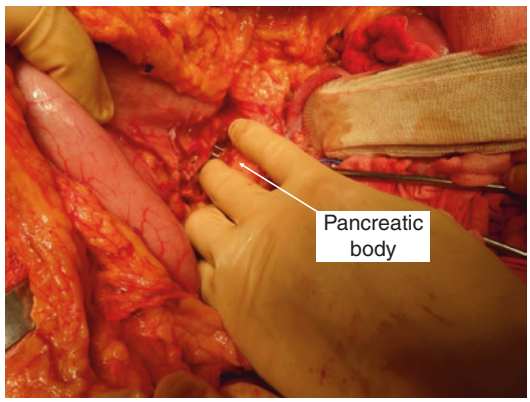

Fig. 17.8 Passage of large forceps. Large Kelly forceps are advanced toward the avascular area above the splenic artery. The avascular area located to the left of the origin of the left gastric artery and superior to the splenic artery should be dissected before passage of the large Kelly forceps

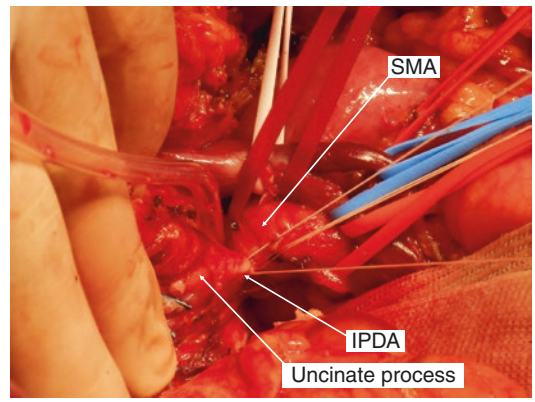

Fig. 17.10 Identification of the IPDA. The SMA is retracted anteriorly, and the IPDA is identified as a string between the SMA and uncinate process and then divided

exposes the inferior vena cava well toward the opposite direction of that seen with the Kocher maneuver, and the left renal vein is exposed through the "Tora-no-Ana."

4. Division of first jejunal artery (FJA) and IPDA

   The jejunum is divided using a stapler. Metastatic lymph nodes have been reported to exist along the FJA [11]. Therefore, we usually dissect the proximal part of the FJA with the regional lymph nodes. The mesentery is divided along the FJA; then dissection around the SMA is advanced. Note that the nerve plexus around the SMA should be preserved. The FJA and IPDA are divided at their origin from the SMA. The IPDA often forms a common trunk with the FJA [12], and in some cases, there are two IPDAs. If identifying the IPDA is difficult, the SMA may be retracted anteriorly by the tape, and the IPDA is identified as a string arising from the posterior wall of the SMA toward the uncinate process of the pancreas (Fig. 17.10). When the IPDA arises from the SMA close to its root, the hanging maneuver of the pancreatic body may help to identify the origin of the IPDA.

5. Division of the GDA

   The stomach or duodenum is divided using a stapler. The left hepatic artery, proper hepatic artery (PHA), common hepatic artery

(CHA), and GDA are taped (Fig. 17.11). If the vascular wall of the GDA is fragile, for instance, in patients after neoadjuvant chemoradiation or cancer extending close to the origin of the GDA, ligation of the GDA may be avoided. Instead, the CHA, PHA, and GDA are occluded temporally with clamps, the GDA is transected sharply, and the stump is closed with two-way running sutures.

6. Division of the pancreas

The splenic vein is taped, and the Penrose drain for the hanging maneuver is passed inside the splenic artery and vein so that the Penrose drain holds the pancreatic body. The cutting line of the pancreas is usually between the origin of the splenic artery and left border of the SMA (Fig. 17.12). We consider that the portion of the SMA margin should be removed with the entire specimen because the SMA margin is the most common site of positive margins. This extensive cutting line does not cause significant deterioration of the endocrine and exocrine functions of the remnant pancreas. Strasberg et al. [13] advocate performing a whipple at the splenic artery, and our concept is similar with theirs. In cases requiring segmental resection of the PV or SMV, we do not attempt to free the splenic vein from the pancreatic parenchyma. After division of the pancreas, the splenic vein is clamped with two pairs of vascular forceps and then divided (Fig. 17.13). The distal stump of the splenic vein is closed with a running suture.

7. Division of the common bile duct

The common bile duct is divided above the confluence of the cystic duct. A drainage tube is inserted into the upper intrahepatic bile duct for intraoperative bile drainage to avoid cholestasis (Fig. 17.14). For neoadjuvant treatments, we encourage our endoscopic colleagues to use metallic stents for better drainage and ask them to place the stents below the bifurcation of the right and left hepatic ducts to enable division at the upper margin of the stent.

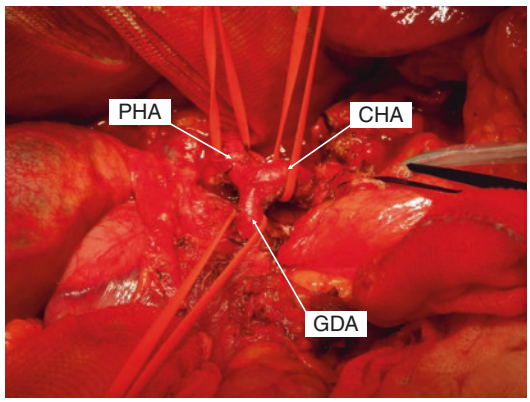

Fig. 17.11 Dissection around the CHA, PHA, and GDA. The lymph nodes around the CHA, PHA, and GDA are dissected, and these arteries are taped

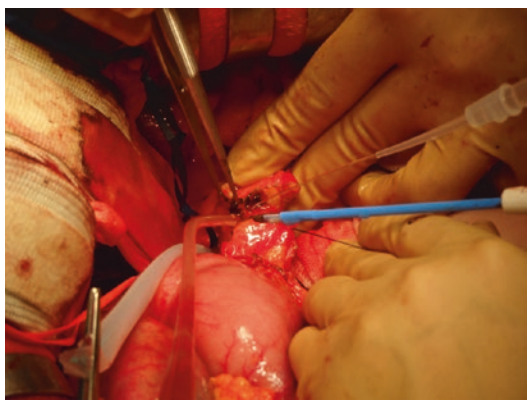

Fig. 17.12 Division of the pancreatic body. The pancreatic body is divided through cautery. During division, cold saline is sprayed onto the cutting surface to reduce thermal damage to the pancreatic duct by cautery

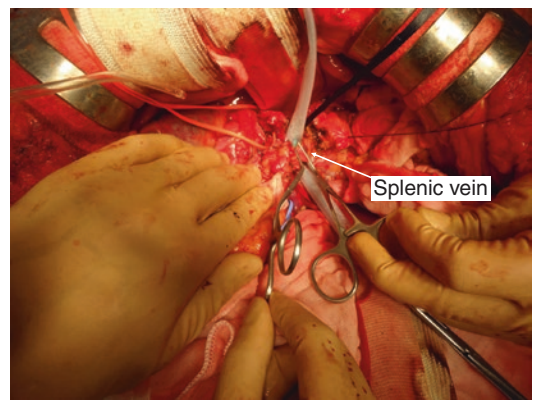

Fig. 17.13 Division of the splenic vein. After division of the pancreatic parenchyma, the splenic vein is clamped with two pairs of vascular forceps and then divided

8. En bloc resection

The duodenum and upper jejunum are fully mobilized and pulled into the right side of the SMA and SMV. The nerve plexus between the pancreas head and celiac artery is divided, and the specimen is fully mobilized except for the SMV and PV (Fig. 17.15). The SMV and PV are divided between two pairs of vascular forceps when tumor invasion to PV/SMV is suspected (Fig. 17.16) and the entire specimen is removed (Fig. 17.17). The SMV and PV are anastomosed end-to-end with continuous suture (Fig. 17.18). Interposition grafts are

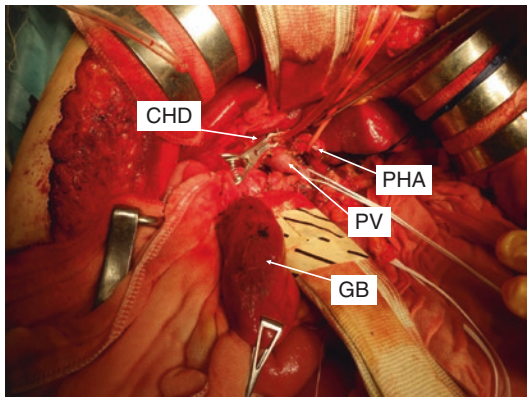

Fig. 17.14 Division of the common bile duct. The common bile duct is divided above the bifurcation of the cystic duct. A drainage tube, albeit optional, is inserted into the intrahepatic bile duct for intraoperative bile drainage. CHD, common hepatic duct; GB, gallbladder

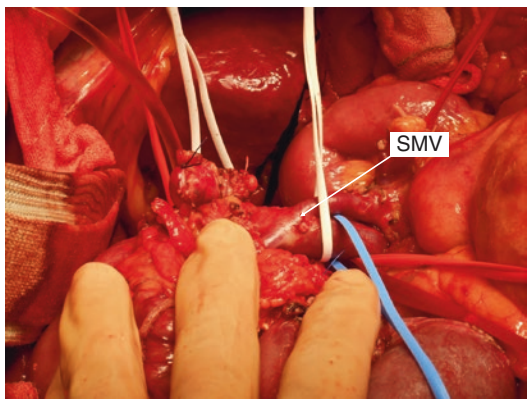

Fig. 17.15 Specimen after dissection. The specimen, including the pancreatic head, is dissected free from the surrounding organs and tissues except for the SMV and PV

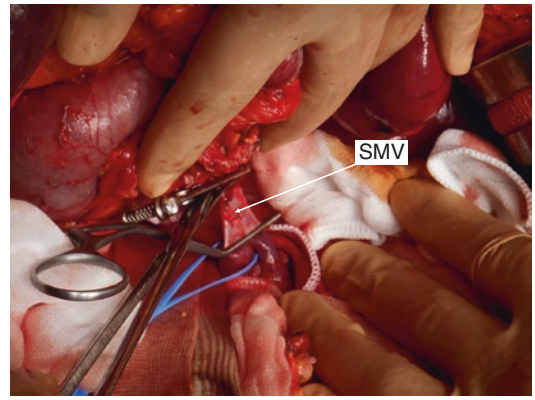

Fig. 17.16 Division of the SMV. The SMV is isolated using vascular forceps. The specimen side also is occluded with a clamp. The SMV is divided along the clamp

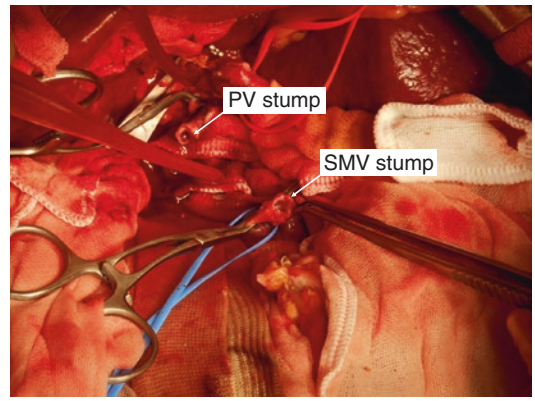

Fig. 17.17 Specimen removal. The PV is clamped with vascular forceps and divided in the same way as the SMV, and the specimen is removed

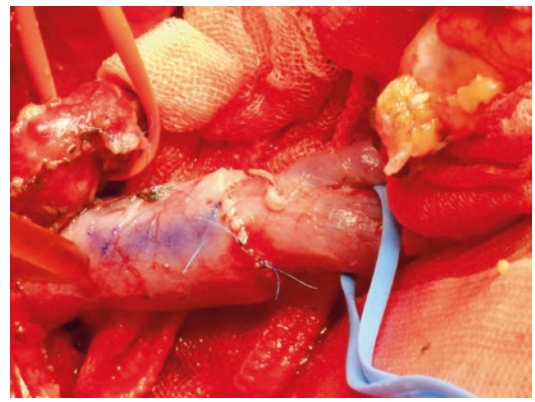

Fig. 17.18 PV reconstruction. End-to-end anastomosis of the SMV and PV is performed

sometimes necessary if the cutting distance of PV/SMV is long to avoid late-onset stenosis. When the confluence of the SMV and splenic vein has tumor involvement, the distal splenic vein is usually left divided and never reconstructed.

17.3 Discussion

The SMV can be safely resected in PD for periampullary pancreatic cancer. A contraindication for resection is arterial involvement [14]. With the standard dissection approach, SMA involvement is often identified at the end of the operation, which often results in resection with positive margins [15].

In our series with routine utilization of the "artery-first" approach, the ratio of R0 resection was 88%, and the average intraoperative blood loss was 1245 mL. Initial diagnoses of Union for International Cancer Control Stages III and IV were made in 13% and 5% of patients, respectively, and the pathological T classifications were T3 and T4 in 76 and 1.3%, respectively [16]. Evaluating the extent of contribution of "artery-first" PD to reduce blood loss is difficult because new vessel sealing system also seems to contribute to reduce the blood loss. In this cohort, we also could not determine whether "artery-first" PD contributed to patient survival because of better locoregional control.

We have learned so much from the disappointing results of previous RCTs, which compared extended versus standard resections [17]; hence, our present concept is to preserve the nerve plexus around the SMA to avoid intractable diarrhea. In case of suspected invasion into the nerve plexus, we use high fractions of neoadjuvant intensity-modified radiation therapy combined with full-dose gemcitabine. Following this concept of preserving the nerve plexus around the SMA has helped us manage postoperative diarrhea in all our patients.

After neoadjuvant chemoradiation, inflammatory reactions may occur around the irradiated tissues. In such a difficult situation, "artery-first" PD may contribute to reduce blood loss and develop an appropriate dissection plane. Using the "Tora-no-Ana" approach, the SMA was easily palpable even in obese patients. The hanging maneuver of the pancreatic body also contributes to make a good operative view around the SMA even in obese patients. In conclusion, the present technique of "artery-first" PD is feasible if the surgical principles of the "Tora-no-Ana" approach and the hanging maneuver of the pancreatic body are followed.

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18 RAMPS Procedure for Adenocarcinoma of the Body and Tail of the Pancreas: How I Do It

Suefumi Aosasa, Makoto Nishikawa, Mayumi Hoshikawa, Takuji Noro, and Junji Yamamoto

18.1 Introduction

Radical antegrade modular pancreatosplenectomy (RAMPS) is performed for cancers of the body and tail of the pancreas, and Strasberg et al. first reported it [1, 2]. This procedure enables surgeons to achieve negative posterior margins more frequently than the traditional left-to-right surgical approach, by facilitating good visibility, dissection of lymph nodes, and tumor isolation following early arterial severance. Kitagawa et al. [3] reported a satisfactory survival rate for modified RAMPS when approaching the anterior renal fascia from the left side. During RAMPS, the dissection commences and advances from right to left, with early division of the neck of the pancreas and splenic vessels. The superior mesenteric artery (SMA) is then dissected from right to left up to its origin at the aorta after tilting the pancreatic stump to the right. Therefore, determination of SMA involvement is impossible without first performing these irreversible operative steps, despite the fact that SMA involvement generally indicates unresectable disease [4, 5].

Our method [6] involves an infra-mesocolic SMA first approach for trial dissection of the SMA. This method is useful for estimating resectability by exposing and taping the SMA prior to the division of the neck of the pancreas.

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18.2 Procedure

18.2.1 Incision

Usually, the abdomen is accessed via a median incision in the upper to middle abdomen. An L-shaped incision is also suitable in obese patients.

18.2.2 SMA First Approach

After the abdominal cavity has been explored to exclude extrapancreatic metastases, the omentum and transverse colon are superiorly retracted. The small intestine is retracted to the right, and the peritoneum is incised at the duodenal recess (Fig. 18.1). After dissecting the mesocolon and left retroperitoneum, the aorta, inferior vena cava, and left renal vein are exposed by mobilizing and rotating the fourth portion of the duodenum and the uncinate process of the pancreas. These procedures expose the left aortic wall and left adrenal gland. The mesentery base is then incised, the ligament of Treitz is opened on the left and anterior side of the mesenteric root, and the duodenojejunal flexure is pulled down. After

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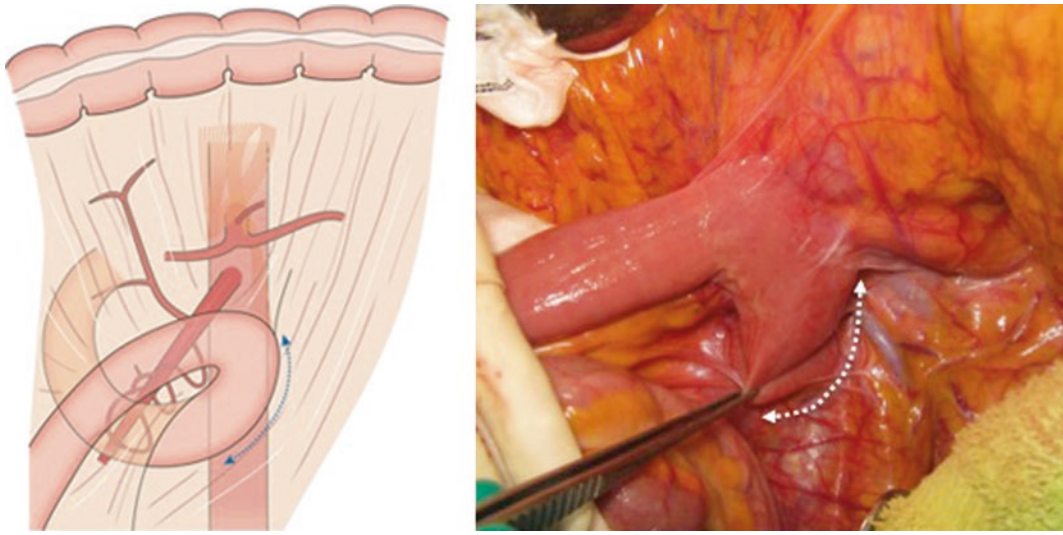

Fig. 18.1 The omentum and transverse colon are superiorly retracted, and the small intestine is retracted to the right. The peritoneum is incised at the duodenal recess (*broken line*)

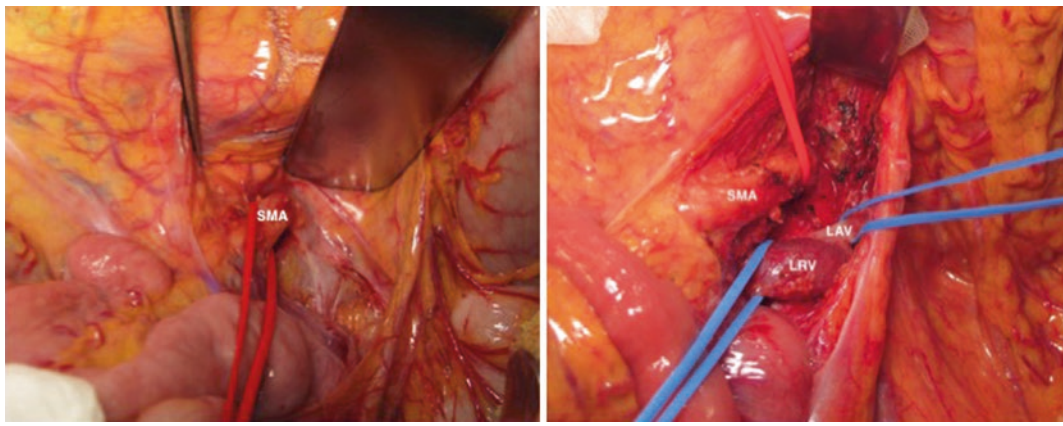

Fig. 18.2 The ligament of Treitz is opened and divided on the left and anterior side of the mesenteric root, and a vessel loop is passed around the superior mesenteric artery (SMA). The dissection proceeds up to the origin of the SMA. *LAV* left adrenal vein, *LRV* left renal vein

these procedures, the SMA is identified, and a vessel loop is passed around the SMA. Then, the dissection of the SMA proximally proceeds to its origin (Fig. 18.2), and the tumor-SMA relationship is assessed.

18.2.3 Exposure of the Superior Mesenteric Vein (SMV)

The transverse colon is pulled downward, and the anterior layer of the gastrocolic ligament is incised, opening the omental bursa. The stomach is then lifted anteriorly. By dissecting the inferior border of the pancreas to the right, the SMV is exposed, and the mesocolon is opened on the left side of the SMA. The middle colic vein is severed if the tumor has invaded this vessel.

18.2.4 Dissection of the Gastroduodenal Lymph Nodes and Division of the Pancreas

After opening the lesser omentum, by dissecting the lymph nodes along the common hepatic artery (CHA) toward the celiac axis (CA), the origin of

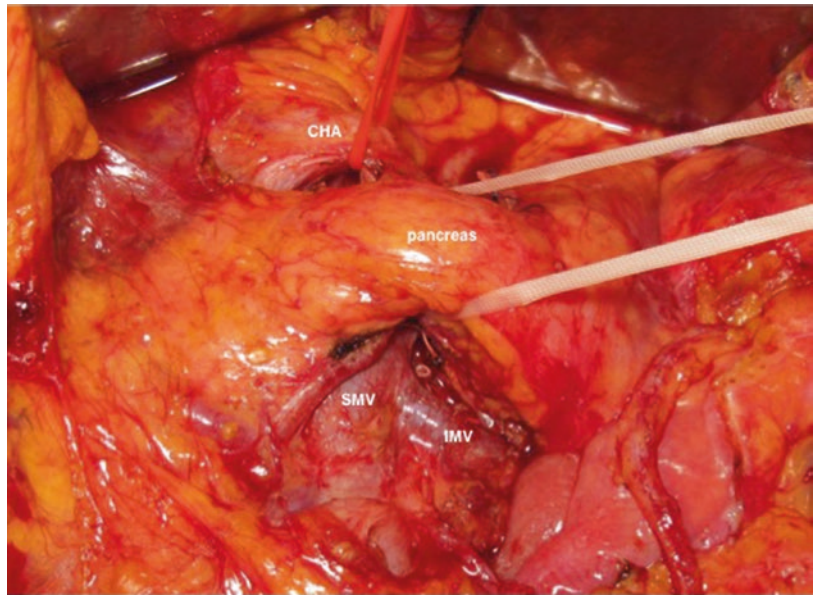

Fig. 18.3 A vessel loop is passed around the common hepatic artery (CHA). The portal vein is exposed along the superior border of the pancreas, and the neck of the pancreas is tunneled above the superior mesenteric vein (SMV). *IMV* inferior mesenteric vein

the splenic artery is confirmed, and the artery is divided at its origin. After lymphadenectomy with skeletonization of the CHA and distal CA, the portal vein is exposed and the neck of the pancreas is tunneled above the SMV (Fig. 18.3). After evaluation using intraoperative ultrasonography to ensure an appropriate pancreatic transection line, the pancreas is divided using a linear stapler with bioabsorbable felt, and the splenic vein is identified and divided at its origin. The distal stump of the pancreas is turned over to the left in order to facilitate lymph node dissection around the CA. The anterior surface of the exposed SMA is located, and if necessary, the vessel is proximally dissected until reaching its origin (Fig. 18.4).

18.2.5 Mobilization of the Left Kidney and Dissection of the Retropancreatic Tissue

The parietal peritoneum at Monk's white line is incised, and the left kidney along with the left side of the colon, left side of the pancreas, and spleen are mobilized en masse. The mobilization is performed until the left side of the lumbar vertebra can be reached. A good surgical view is obtained by placing surgical towels behind the left kidney [7]. The stump of the distal pancreas is retracted to the left, and the dissection along the SMA is extended toward the left side to the aorta and the left renal vein. Retroperitoneal dissection is partially performed in advance during the initial procedures via an infra-mesocolic approach. The surgeon should be able to easily locate the right plane and complete the dissection from the aorta, adrenal gland, kidney, diaphragm, and retroperitoneal muscles. The inferior mesenteric vein is severed if it connects to the splenic vein. The dissection line depends on whether the left adrenal gland is preserved (Fig. 18.5). After the Gerota's fascia is cut and the retropancreatic soft tissues, including the lymph nodes, are dissected, the resection is completed.

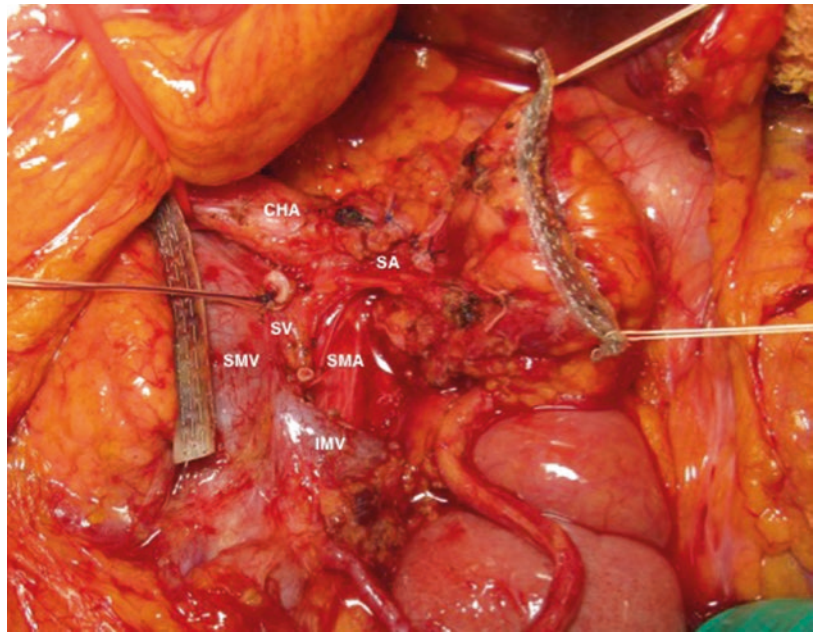

Fig. 18.4 After the division of the splenic artery (SA) at its origin, the pancreas is divided using a linear stapler with bioabsorbable felt and is tilted to the left. The splenic vein (SV) is divided at its origin. The anterior surface of the superior mesenteric artery (SMA) is already exposed. *CHA* common hepatic artery, *SMV* superior mesenteric vein, *IMV* inferior mesenteric vein

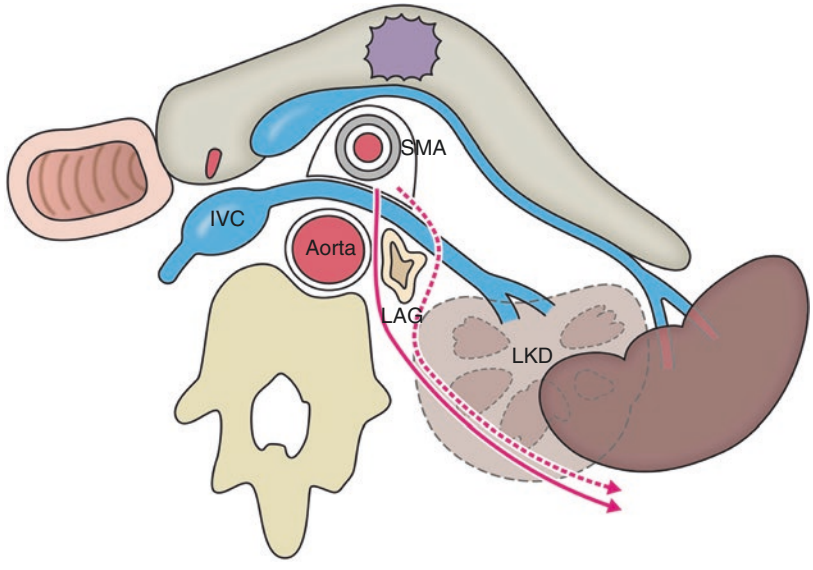

Fig. 18.5 Transverse view schema showing the dissection line of the combined resection (*solid line*) and the preservation (*broken line*) of the left adrenal gland (LAG). *SMA* superior mesenteric artery, *IVC* inferior vena cava, *LKD* left kidney

Conclusion

Our method provides an approach for critical dissection in order to determine resectability. Dissection furthers up along the aorta to expose the left renal vein, and the left adrenal gland can help prepare the RAMPS right dissection plane in advance. The infra-mesocolic SMA first approach provides a reliable and safe introduction to RAMPS.

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19 The Modified Appleby Procedure for Locally Advanced Pancreatic Body/Tail Cancer: How I Do It

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19.1 Introduction

Tumors of the body and tail account for approximately one-third of pancreatic cancers, and up to three-quarters of body and tail tumors are deemed unresectable on presentation [1]. Unresectability is a result of liver metastases, carcinomatosis, or local invasion of major vascular structures. Although pancreatectomy in the presence of metastatic disease has not proven beneficial, resection of locally advanced pancreatic cancer to negative margins may improve survival [2]. Treatment of locally advanced pancreatic adenocarcinoma with arterial involvement remains controversial; however, 30% of patients with locally advanced, Stage III pancreatic cancer will die without evidence of metastatic spread [3]. As such, this group of patients is most likely to benefit from an aggressive surgical approach. Neoadjuvant therapy has allowed for more careful selection of patients that may benefit from pancreatectomy with arterial resection.

Whereas locally advanced pancreatic head adenocarcinoma may invade the superior mesenteric artery, locally advanced cancers of the body and tail of the pancreas will often first invade the celiac axis or common hepatic artery. Under carefully selected circumstances, patients may undergo the modified Appleby procedure for celiac axis or common hepatic artery involvement. The Appleby procedure was originally proposed in 1953 as a treatment for locally advanced gastric cancer with bulky celiac lymphadenopathy, and consisted of en bloc resection of the celiac axis, total gastrectomy, and distal pancreatectomy with splenectomy [4]. Nimura et al. [5] in Japan first modified the procedure for advanced pancreatic cancer of the body/tail in 1976. The modified procedure consisted of distal pancreatectomy with celiac axis resection (DP-CAR). Pancreatectomy with en bloc arterial resection was introduced in the Western world by Fortner [6] around the same time; however, poor long-term survival and high morbidity led this technique to fall out of favor. It wasn't until the early 2000s that the modified Appleby procedure was endorsed in the Western world. Our group, Gagandeep et al. [7], previously demonstrated that resection of the celiac axis with or without reconstruction could be done safely with acceptable postoperative mortality. The procedure has gained more favor in recent years as morbidity with pancreatic surgery has improved, selection criteria have improved, and several major centers have shown promising results [8–10]. Furthermore, patients with locally advanced pancreatic body/tail cancer involving the celiac plexus may suffer severe

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pain, leading to a poor quality of life. The modified Appleby procedure may palliate symptoms of pain in addition to potentially providing a survival benefit.

19.2 Diagnosis

Preoperative imaging is paramount for determining resectability of pancreatic cancer and for properly planning the appropriate operation for a pancreatic mass. Computed tomography (CT) or magnetic resonance imaging (MRI) with multiphase pancreatic protocol is preferred for evaluation of local invasion associated with a pancreatic mass (Fig. 19.1). The role of positron emission tomography (PET)/CT currently is not clear in the staging of pancreatic adenocarcinoma, and PET/CT is not a mandatory examination for staging; however it may be used after performance of pancreas protocol CT imaging in high-risk patients to evaluate for metastatic disease [11]. For patients in whom neoadjuvant therapy is being considered, biopsy for proof of malignancy is required; however biopsy proof of malignancy is not mandatory if initial surgical resection is being entertained.

Special attention should be paid to the celiac axis and the superior mesenteric artery (SMA) on imaging. The liver not only receives arterial blood flow from the common hepatic artery from the celiac axis but also receives collateral blood flow through the head of the pancreas from the inferior pancreaticoduodenal arteries coming from the SMA flowing through the gastroduodenal artery (GDA). The SMA should be widely uninvolved, and the celiac axis must have a sufficient segment of normal artery to allow for safe transection at the takeoff from the aorta (Fig. 19.2). In addition, the common hepatic artery must have enough space to before the takeoff of the GDA. Replaced hepatic vessels should be noted prior to surgery to plan accordingly.

The patient's presenting symptoms may also suggest involvement of adjacent structures by disease, and this can be confirmed on imaging. Gastric outlet obstruction or back pain may suggest a locally aggressive tumor with invasion of the stomach or the celiac plexus/retroperitoneum, respectively.

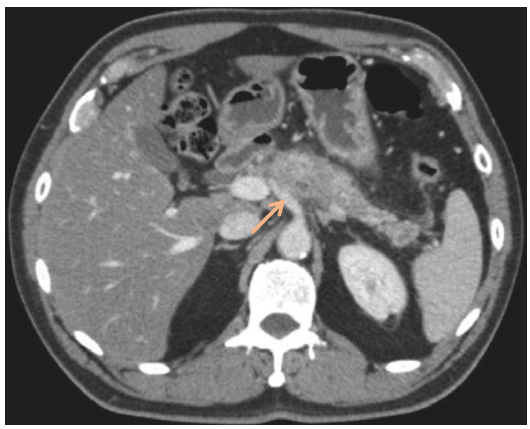

Fig. 19.1 Locally advanced pancreatic body adenocarcinoma on preoperative CT scan. The celiac axis is invaded by tumor (*arrow*)

19.3 Patient Selection

The indication for the modified Appleby procedure is involvement of the celiac axis by a pancreatic body tumor without involvement of the head of the pancreas or SMA. In general, only a minority of patients are candidates for this aggressive operation. In our series, the modified Appleby procedure was performed in only 2% of patients undergoing pancreatectomy during the study period; however, the frequency of the operation has increased with time at other institutions [7, 12]. With proper selection, surgery may be successfully performed in up to 87% of patients preoperatively deemed resectable with a modified Appleby procedure [8]. Patients are selected based on their likelihood of obtaining negative margins, response to neoadjuvant therapy, lack of distant metastases, and functional capacity.

The treatment of pancreatic adenocarcinoma may require multiple modalities, and a component of patient selection may also involve the use of neoadjuvant therapy. By using a neoadjuvant treatment approach, patient selection may be further refined to those patients who will most

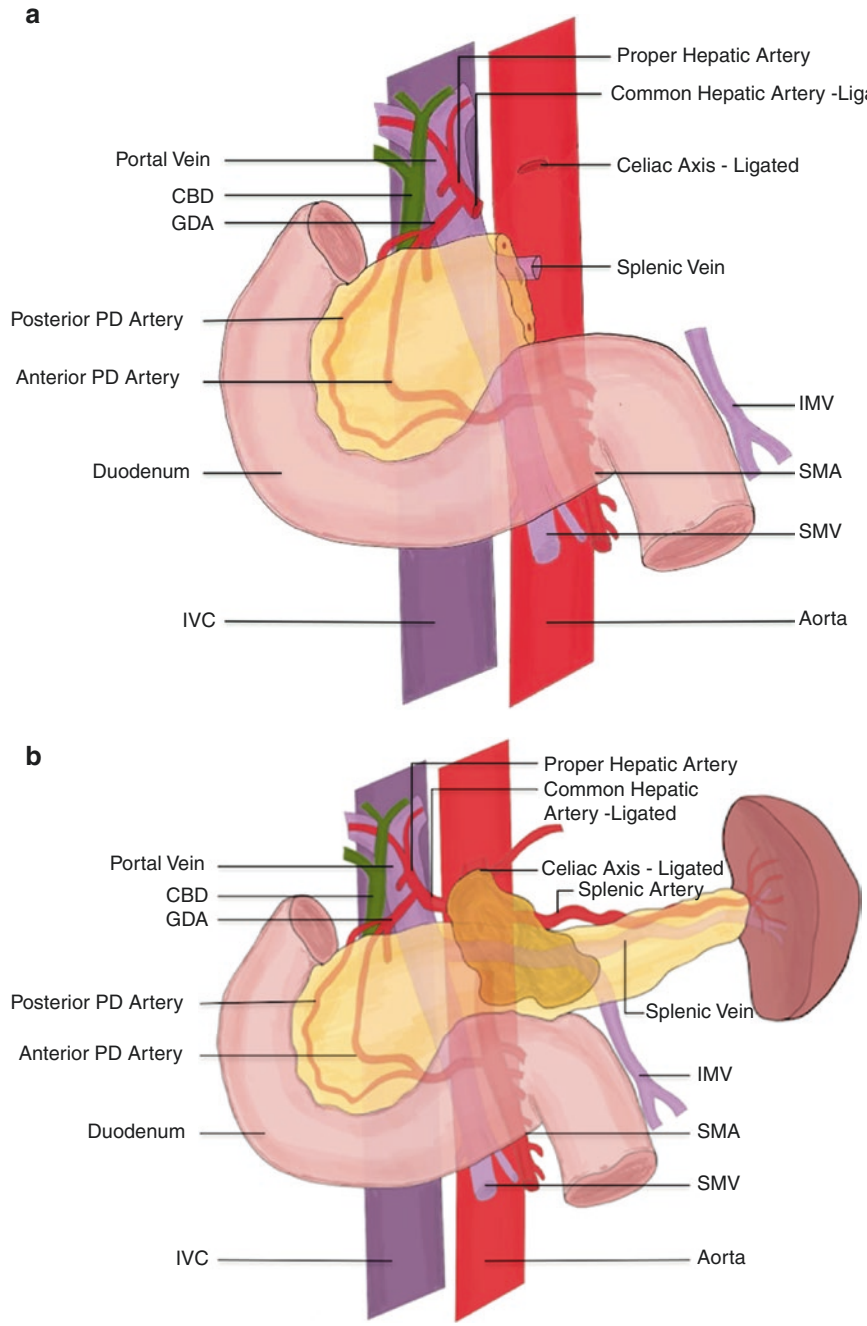

Fig. 19.2 (**a**) Illustration of a locally advanced tumor of the body of the pancreas. Tumor involves the celiac axis. (**b**) Anatomy after modified Appleby procedure. Ligation of the common hepatic artery and celiac axis are required. Blood flood to the liver is based on collaterals from the superior mesenteric artery to the gastroduodenal artery. *CBD* common bile duct, *GDA* gastroduodenal artery, *PD* pancreaticoduodenal, *IVC* inferior vena cava, *IMV* inferior mesenteric vein, *SMA* superior mesenteric artery, *SMV* superior mesenteric vein

benefit from a major resection. Approximately 20% of patients with locally advanced pancreatic adenocarcinoma are considered surgical candidates using this strategy, thus eliminating those patients who would not benefit from a major operation [8].

19.4 Surgical Technique

A safe and efficient operation is ensured by adequately selecting the ideal patient for a modified Appleby procedure. Locally advanced pancreatic cancers are at risk of undiagnosed metastases; therefore, a diagnostic laparoscopy is advisable at the time of the planned resection. A laparotomy incision is made once the liver and the peritoneal surfaces have been examined without evidence of metastatic disease. We prefer a bilateral subcostal incision because this allows access to the pancreas in its entirety, the spleen, and the porta hepatis; however, a midline incision may also be used.

19.4.1 Determining Resectability

Diagnostic laparoscopy is usually not enough to provide enough information to determine resectability. The pancreas must be fully examined by opening the lesser sac and performing an extended Kocher maneuver. The pancreas is examined to appreciate the mass in relation to vital structures, with particular attention paid to the celiac axis, SMA, and GDA. The fundamental principle underlying the operation requires flow to the liver from collaterals through the pancreatic head from the SMA to the GDA (Fig. 19.2). In our early experience, we would perform an angiogram to confirm good collateral circulation; however, we subsequently feel that angiography is not necessary after observing very little variation in the well-preserved blood supply through the head of the pancreas. Once adequate exposure is obtained, resectability is ultimately determined by clamping the common hepatic artery and verifying blood flow to the proper hepatic artery and liver via the GDA. In the case of poor blood flow, the common hepatic artery may be reconstructed to restore blood flow if the tumor can still be safely removed off of the aorta.

19.4.2 Dissection of the Celiac Trunk

The celiac trunk is accessed both anteriorly and posteriorly. By performing a cholecystectomy and portal node dissection, the proper hepatic artery, GDA, and common hepatic artery can be identified and traced to the level of tumor involvement. Once the common hepatic artery is isolated with a vessel loop, the common hepatic artery is clamped to verify flow from the GDA into the proper hepatic artery. It is at this point that the extent of celiac axis involvement is often appreciated.

Attention is then turned to separation of the transverse mesocolon from the omentum by entering the lesser sac. The gastrocolic ligament is divided followed by the lienocolic ligament allowing for caudal retraction of the colon. The peritoneum along the inferior border of the pancreas is incised, and the pancreas and spleen are lifted up from the retroperitoneum in the avascular plane. We divide the distal splenic artery early to allow the spleen to decompress. The dissection of the pancreatic body/tail starts at the inferior border of the spleen, followed by division of the lienorenal and lienophrenic ligaments, and then this dissection is carried over until the pancreas is completely freed from the retroperitoneum up to the superior mesenteric vein (SMV) and PV.

Posteriorly, the celiac artery is approached in one of two ways. If the PV can be completely freed from the neck of the pancreas, the pancreas may be divided allowing access to the base of the celiac trunk. The surgeon should be committed to the operation prior to dividing the pancreas. Taking down the attachments of the spleen and distal pancreas may also expose the aorta and takeoff of the celiac trunk. The spleen and distal pancreas are rotated medially while separating the avascular plane posterior to the pancreas. From here, both the celiac artery and SMA are identified. The SMA is examined for any tumor involvement and then freed from any attachments to the body of the pancreas. The celiac artery is examined for extent of tumor involvement and is completely encircled. A vascular clamp is placed across the base of the celiac artery, and blood flow to the liver and stomach are again assessed.

Following this, fluorescein is injected intravenously, and the perfusion of the liver and stomach are visualized using fluorescent imaging. This can be done at any point where the operation is deemed at a point of no return. There must be a small cuff of uninvolved celiac artery to allow for safe ligation. In preparation for ligation, the pancreas is divided

anterior to the PV and SMV with a stapler if this has not already been done. Any involved stomach should be resected en bloc with the specimen.

19.4.3 Vascular Division

Division of the celiac axis is the last step of the operation. In addition to division of the pancreas, the splenic vein is clamped, transected, and oversewn with 5-0 polypropylene suture. This maneuver allows full visualization of the celiac trunk. A clamp is placed across the takeoff at the aorta, and the celiac artery is divided and oversewn with 5-0 polypropylene sutures. Following this, the common hepatic and left gastric arteries are ligated and oversewn, again with 5-0 polypropylene suture. The specimen is removed at this point and sent for frozen section (Fig. 19.3). The stump of the pancreas is oversewn with 4-0 polypropylene sutures. Alternatively, the vessels may be transected using a stapler if there is enough room on the artery to allow for this technique.

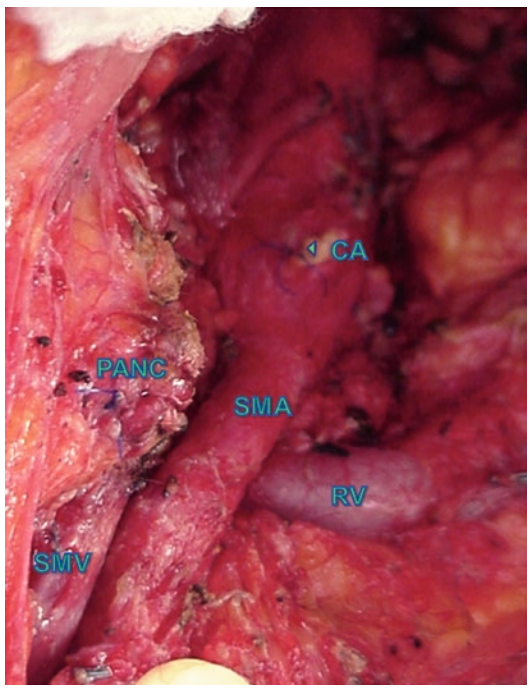

Fig. 19.3 Intraoperative images after resection. *PANC* pancreas (cut), *SMA* superior mesenteric artery, *SMV* superior mesenteric vein, *PV* portal vein, *RA* left renal vein

The blood flow to the liver and stomach are again assessed. If either structure appears ischemic, vascular reconstruction should be performed. Fluorescein may be injected again to reassess for ischemia after vascular division. Ischemia should usually be evident in the time it takes for pathologic margin assessment.

Vascular reconstruction may be done in a number of ways. Primary anastomosis between the left gastric artery or the common hepatic artery and the celiac stump is performed if mobilization of the vessels allows for a tension-free anastomosis. A reconstruction with saphenous vein graft may be preferred if a primary anastomosis is not possible. The area should be well drained to prevent pancreatic enzymes from sitting around the vascular anastomoses.

19.5 Complications

Complications associated with the modified Appleby procedure include the risks inherent to pancreatic surgery as well as risks specific to arterial resection [13]. Major complications may reach 35–41% [12–14]. The most common complication is pancreatic fistula. Nakamura et al. [13] reported a fistula rate, grade B or C, of 33%. In comparison, pancreatic fistula may be seen in up to 30% of patients undergoing distal pancreatectomy [15]. This is followed by ischemic gastropathy (29%), which in the most serious of circumstances may lead to perforation (6%). The usual result of gastric ischemia is delayed gastric emptying. Ischemia of the liver may lead to hepatic infarction and ultimately liver abscess. To minimize the risk of ischemic complications, perfusion of the liver and stomach may be assessed in two ways: (1) injection of fluorescein and (2) assessment of mean arterial pressure (MAP) from the hepatic and left gastric stumps, alth ough t his is more tedious than fluoroscein. A drop in MAP of >25% is used by some as criteria for arterial reconstruction to minimize ischemia [16]. While complications may be minimized, patients should be extensively counseled preoperatively to understand the inherent risks associated with DP-CAR.

19.6 Outcomes

Vascular resection for pancreatic adenocarcinoma was first introduced in the 1970s in the both the East and West [5, 6]. Enthusiasm from Western surgeons was initially lacking, and vascular resection fell out of favor due to high perioperative mortality. More recent institutional series have reported more favorable outcomes (Table 19.1). A meta-analysis from Mollberg et al. in 2011 reported higher perioperative mortality and worse oncologic outcomes with DP-CAR compared with DP alone [17], but more recent series in the era of neoadjuvant therapy have reported improved results [8, 9, 12, 13]. This likely reflects a refinement in the patient selection process, selecting patients who are fit and who have responded well to neoadjuvant therapy without the development of progressive and/or metastatic disease. A limitation of the meta-analysis was study heterogeneity. The evaluation included patients who were operated on over a three-decade period, with most operations performed prior to 2000, who underwent both venous and arterial resection, and included patient having undergone SMA resection and reconstruction. In contrast, the largest, single-institutional series from Nakamura and colleagues of 80 patients undergoing arterial resection reported 30-day mortality of 1.3% and in-hospital mortality of 5% [18]. The report included patients treated with and without chemotherapy both in the adjuvant and the neoadjuvant setting. The largest studies to date using neoadjuvant therapy are by Christians et al. [8] and Peters et al. [12] (Table 19.1). There were no perioperative deaths in these series of 15 and 17 patients, respectively, showing that DP-CAR can be safely performed in patients who are properly selected.

A recent analysis of data from National Surgical Quality Improvement Project (NSQIP) Pancreatectomy Demonstration Project reviewed survival across multiple treatment settings. In patients undergoing DP-CAR, mortality with celiac arterial resection was as high as 10% compared to 1% in patients undergoing DP alone [14]. While 10% mortality is not prohibitively high for an otherwise fatal condition, the high mortality in comparison to DP alone underscores the importance of performing the operation in a tertiary, multidisciplinary center. In the properly selected patient, perioperative risk may be minimized, and more aggressive surgery may be warranted in the setting of neoadjuvant chemotherapy.

Table 19.1 Reported series of modified Appleby procedure in the setting of neoadjuvant therapy

First author	Year	Number of patients undergoing AR	30-day mortality (%)	Follow-up/survival	Comments
Cesaretti [9]	2008–2013	7	0	Median survival 24 months (5 patients who underwent surgery)	7/7 (all patients also underwent CA coiling, 2 patients progressed)
Nakamura [13]	1998–2015	80	1.3 (5)[a]	Median survival 30 months	11/80 preoperative chemotherapy
Christians [8]	2011–2013	15	0	Median follow-up 21 months (9–38 months). Five recurrences, all AWD	2 patients unresectable, 14/15 preoperative chemotherapy
Peters [12]	2004–2016	17	0	Median survival 20 vs 19 months (DP-CAR vs DP, p = 0.76)	15/17 preoperative chemotherapy
Mollberg (meta-analysis) [17]	1974–2009	366 (12.6)[b]	0–45	Median survival 8.5–20 vs 12–25 months (DP-CAR vs DP)	Significant heterogeneity and bias

[a]Nakamura et al. report 30-day mortality of 1.3% and mortality during initial hospitalization of 5%
[b]The meta-analysis included a total of 366 patients from 26 studies, with a median of 12.6 patients per study
DP-CAR distal pancreatectomy, celiac axis resection, *DP* distal pancreatectomy, *CA* celiac axis, *AR* arterial resection, *AWD* alive with disease

Long-term survival after R0 resection with the modified Appleby procedure is improved compared with patients treated with chemotherapy alone. The median survival of patients with unresectable locally advanced disease ranges from 8.4 to 13 months [19–22]. The prognosis of patients with unresectable locally advanced pancreatic cancer is similar to patients with metastatic disease. The median survival in patients with metastatic disease treated with FOLFIRINOX chemotherapy is approximately 11 months [23]. In a study comparing gemcitabine and nab-paclitaxel to gemcitabine alone, which included patients with locally advanced disease, median overall survival for the study group was 8.5 months [24].

Long-term survival after pancreatectomy with arterial resection is similar to patients with resectable disease treated with pancreatic resection, with median survival as high as 31 months in the Japanese literature [18]. The median survival in the most recent Western series consisting of patients receiving neoadjuvant chemotherapy is between 20 and 24 months, with some data limited by short follow-up periods (Table 19.1) [8, 9, 12, 25]. In comparison, similar survival is seen in patients with resectable pancreatic cancer treated with adjuvant therapy. The ESPAC-1, CONKO-001, ESPAC-3, RTOG-9704, and GISTG trials report a median survival of 20.5–24.5 months in patients with resectable pancreatic cancer treated with or without adjuvant chemotherapy after pancreatic resection [26–30]. With multimodal treatment for locally advanced pancreatic cancer, including the modified Appleby procedure, long-term survival may be achieved in patients undergoing a margin negative resection, similar to other patients with resectable pancreatic cancer. These data suggest that patients undergoing DP-CAR do benefit oncologically from an aggressive operation despite the higher perioperative mortality.

Conclusions

Arterial resection in patients with body or tail pancreatic adenocarcinoma should be reserved for carefully selected patients with vascular involvement limited to the celiac axis or common hepatic artery. Preoperative scans should be carefully examined for collateral blood flow to the liver via the SMA and GDA. Neoadjuvant chemotherapy is advisable in all patients considered for the modified Appleby procedure (DP-CAR) with locally advanced pancreatic cancer to select those patients most likely to benefit from a major aggressive resection. With this approach, survival may be similar to patients undergoing a standard pancreatic resection.

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20 Laparoscopic Pancreaticoduodenectomy: How I Do it

Alessandro Paniccia and Barish H. Edil

20.1 Introduction

Minimally invasive pancreaticoduodenectomy (MIPD) is one of the most challenging abdominal operations currently being performed; it demands excellent surgical technique and requires a steep learning curve [1]. Despite the introduction of MIPD in 1994 by Gagner and Pomp [2], this technique remains sparsely utilized—mainly in large academic centers—and no randomized controlled trial exists that compares MIPD with open pancreaticoduodenectomy (OPD). Furthermore, several interpretations of MIPD can be found in the surgical literature, spanning from total minimally invasive techniques (when both the dissection and the reconstruction phase are performed totally laparoscopically) to the most commonly reported hybrid techniques (when the dissection phase is performed laparoscopically and the reconstruction phase is performed via minilaparotomy) [3–10].

The steep learning curve associated with MIPD is often the biggest challenge faced by the surgeon and surgical team [11]. Speicher et al. demonstrated that the operative time correlates closely to the technical difficulties encountered in the first—steep part—of the learning curve. Although this represents the biggest obstacle for the first 10 cases, a significant reduction in operative time is experienced within the first 50 cases after which operative time and estimated blood loss were consistently lower than open pancreaticoduodenectomy [11].

It is apparent that a global trend toward minimally invasive oncologic surgeries is on the rise, and hepatobiliary surgeons—especially in an academic center of excellence—will need to be familiar with the various aspects of minimally invasive pancreaticoduodenectomy.

20.2 Patient Selection

Most patients with pancreatic, ampullary, or biliary pathologies who require a pancreaticoduodenectomy are eligible for a laparoscopic approach. One limitation is represented by patients with locally advanced pathologies (i.e., locally advanced or borderline resectable pancreatic adenocarcinoma) with involvement of the mesenteric vasculature due to the inherent technical difficulties with laparoscopic vascular resection and reconstruction (although a few specialized centers occasionally offer TLP in this setting) [7, 8].

Adequate preoperative imaging is paramount—and its importance cannot be stressed enough—especially in defining any aberrant vascular anatomy, as tactile sensation is lost during a

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laparoscopic procedure. Therefore, having ample anatomic knowledge of the case at hand (e.g., aberrant or replaced right hepatic artery and alike) will avoid intraoperative catastrophe or need for laparotomy.

20.3 Procedure

20.3.1 Dissection Phase

The patient is placed supine on the operating table, and care is taken to properly secure the patient with a thigh belt to the operating table. Care is taken to ensure proper patient positioning and stability, as the table will be tilted at different stages during the procedure to help with organ exposure during tissue dissection and reconstruction. The upper extremity bony prominences are covered with soft pads; both arms are extended to no more than 60° (to avoid injury to the brachial plexus).

The surgeon is positioned on the left side of the patient, the first assistant is positioned on the right side of the patient, and the second assistant stands on the left side of the patient, next to the surgeon. However, it is worth noting that operating is done from both sides of the patient as the procedure moves through its different phases.

The procedure can be performed using five trocars, including a Hassan optical trocar, two 12 mm trocars, and two 5 mm trocars.

The Hassan optical trocar is positioned at the umbilicus (to be used for a 10 mm 30° or 45° angled laparoscope), two 12 mm trocars are placed along both left and right hemiclavicular line approximately 2 cm below the inferior costal margins (these are the two main working ports), one additional 5 mm trocar is placed on the right side of the umbilicus (to provide lateral traction as needed), and an additional 5 mm trocar can be placed on the left of the umbilicus if needed.

The peritoneal cavity is carefully accessed, and the abdomen is thoroughly explored for evidence of metastatic disease; following this mandatory first step, the attention is turned to the identification of the lesser sac. An ultrasonic dissector is used to divide the gastrocolic ligament, below the gastroepiploic vessels, allowing access to the retroperitoneal area and ultimately leading to direct visualization of the pancreas (Fig. 20.1).

Subsequently the assistant provides cephalad traction on the stomach (by grasping the stomach antrum or body with an atraumatic laparoscopic grasper), therefore facilitating the identification of any adhesions present between the posterior surface of the stomach and the anterior surface of the pancreas. These adhesions can then be sharply divided gaining full exposure of the anterior surface of the pancreas.

The dissection of the porta hepatis is initiated, and the gastroduodenal artery (GDA) lymph node is identified and removed. The removal of the GDA lymph node facilitates the visualization of the GDA origin; care is taken to verify that the GDA is properly skeletonized and removed of all surrounding soft tissue in order to ensure full ligation with the surgical clips. During this phase, extreme care is taken to avoid avulsion of the superior anterior pancreaticoduodenal artery.

It is the authors' practice to perform a complete dissection of the common and proper hepatic artery—prior to transection of the gastroduodenal artery—as test occlusion of the gastroduodenal artery and palpation of the proper hepatic are not possible. This extra step will facilitate proper recognition of the GDA and its origin from the common hepatic artery, and it will prevent erroneous and catastrophic ligation of the common hepatic artery.

The GDA can now be ligated; the authors prefer a suture ligation of the proximal GDA that is additionally reinforced with two medium surgical clips, proximally and distally, prior to its sharp division (Fig. 20.2a, b).

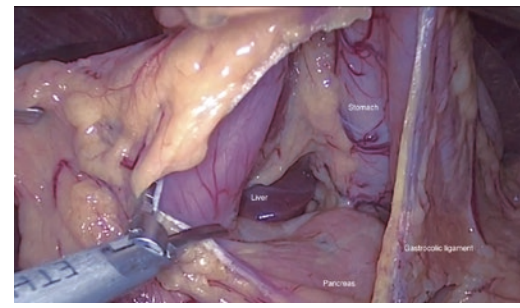

Fig. 20.1 Identification and access to the lesser sac

Attention is then turned to the inferior pancreatic border to identify the superior mesenteric vein (SMV). Blunt dissection is carried on along the SMV anterior surface, progressively separating the posterior aspect of the pancreatic neck from the SMV and eventually leading to the identification of the confluence between the SMV vein and the splenic vein (Fig. 20.3a, b). During this step, the laparoscopic approach offers a tremendous advantage represented by the magnified visualization of the "tunnel" created between the pancreatic neck and the SMV-splenic vein confluence; this is a clear advantage compared to a traditional open procedure.

The hepatic flexure and the transverse colon are mobilized inferiorly after division of the colohepatic peritoneum exposing the second and third portion of the duodenum. An extended Kocher maneuver is performed to allow for medialization of the duodenum, and the plane between the duodenum and the retroperitoneum is identified and dissected using either blunt or energy dissection, ultimately leading to the identification of the inferior vena cava, the aorta, and the superior mesenteric artery.

The gallbladder is identified, the Calot's triangle is exposed, and the cystic duct and the cystic artery are dissected and doubly ligated with surgical clips prior to being sharply divided. A cholecystectomy is then completed in a standard laparoscopic fashion, and the dissected gallbladder is placed in the right abdomen for later removal.

The stomach can then be transected just proximal to the pylorus using a laparoscopic stapling device (the pylorus should be clearly identified prior to the transection to prevent stapling across the pylorus). The gastric remnant can now be mobilized into the left upper abdomen allowing for improved exposure of the pancreas.

The pancreatic neck is then divided along the previously created pancreatic tunnel (with the use of electrocautery), and the pancreaticoduodenal arteries are controlled (with the use of an energy device) for hemostasis (Fig. 20.4a). The pancreatic duct is identified, and an appropriately

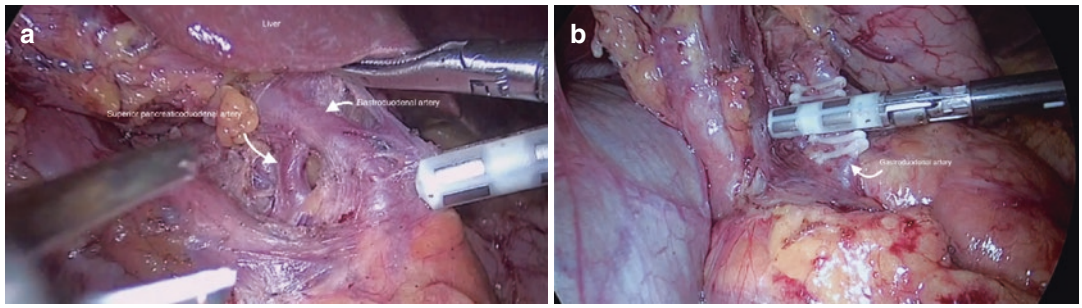

Fig. 20.2 (**a**) Identification and (**b**) ligation of the gastroduodenal artery (GDA)

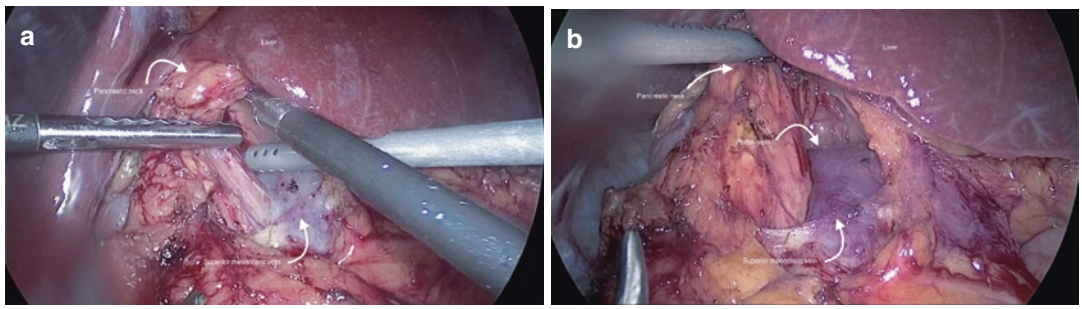

Fig. 20.3 (**a**) Identification and blunt dissection along the anterior surface of the superior mesenteric vein (SMV), (**b**) retropancreatic tunnel with identification of the confluence of the SMV and splenic vein

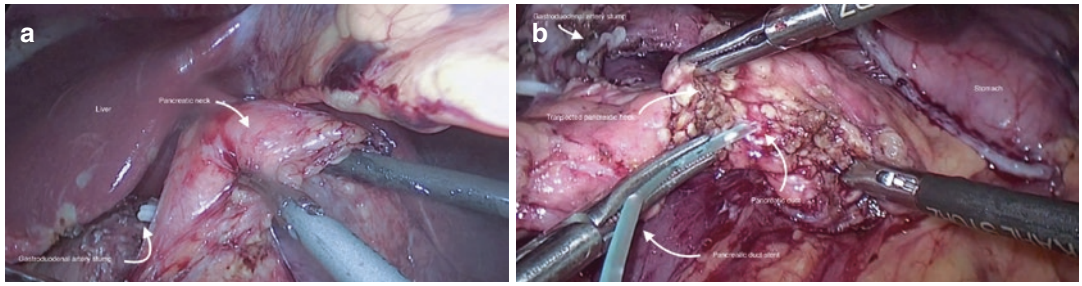

Fig. 20.4 (**a**) Division of the pancreatic neck, (**b**) identification and cannulation of the pancreatic duct with a silicone (4 to 8 Fr) feeding tube

sized pediatric feeding tube (usually ranging from 4 to 8 French) is inserted in the pancreatic duct; this will function as a temporary stent and will aid with the subsequent reconstruction (Fig. 20.4b).

The common bile duct is then identified, dissected free from the surrounding tissues, and its proximal aspect is secured with a surgical bulldog clamp; this will avoid spillage of bile during the remaining steps of the procedure. Electrocautery is then used to transect the common bile duct approximately 2–3 cm above the superior pancreatic border.

The authors use a laparoscopic stapler to divide the jejunum to 50% of its width at the site chosen for the future definitive transection; the division of only half of the jejunum allows for easier rotation of the jejunum through the ligament of Treitz and under the mesenteric vessels.

Alternatively, the jejunum can be completely transected, and the two jejunal free ends can be held together by a stay suture that will eventually allow for easy jejunal rotation under the mesenteric vessels.

Bringing the jejunum through the ligament of Treitz—instead than through a defect in the transverse mesocolon—avoids jejunal twisting that can be easily overlooked laparoscopically and provides a tension-free loop for reconstruction.

The ligament of Treitz is identified and mobilized from its retroperitoneal attachments, using blunt dissection and an energy device. Once the dissection is completed, the duodenum and the jejunum can be safely rotated under the mesenteric vessels. A window is created in the mesentery, approximately 15–20 cm distal to the duodenojejunal flexure, and the jejunal vascular arcades are serially divided with the use of an energy device.

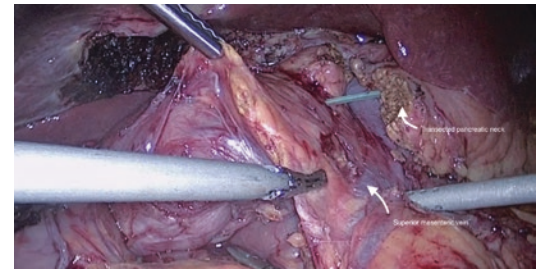

Fig. 20.5 Dissection of the uncinate process from the superior mesenteric vein (SMV)

Attention is then turned to the pancreatic neck with the ultimate goal to expose and to dissect free the uncinate process. The assistant applies gentle cephalad and lateral traction to the pancreatic head (toward the patient's right); this allows the surgeon to perform a blunt dissection along the SMV-portal vein confluence achieving complete separation between these structures and the posterior surface of the remaining pancreas (Fig. 20.5).

At this stage, the uncinate process can be dissected free from the superior mesenteric artery using an energy device; however, occasionally it will require clips or suture ligature. A laparoscopic suctioning device can be used to gently retract the superior mesenteric vein laterally (toward patient's left side) allowing for complete visualization of the attachment between the SMA and the uncinate process. It is paramount to simultaneously visualize both vessels (SMV and

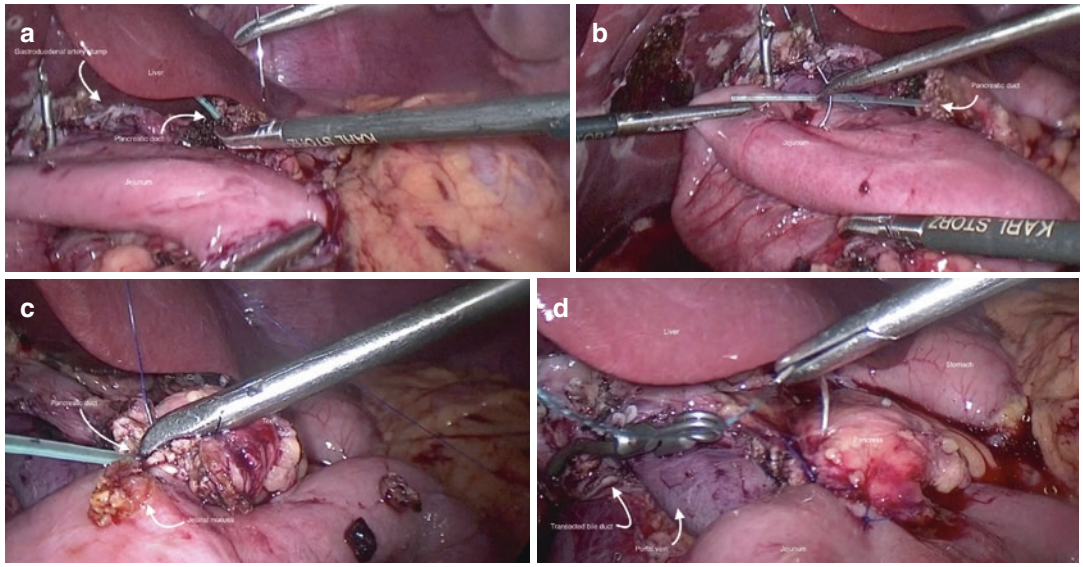

Fig. 20.6 End-to-side, duct-to-mucosa pancreaticojejunostomy construction: (**a** and **b**) posterior row, (**c**) pancreatic duct to jejunal mucosa anastomosis, (d) anterior row

SMA) during this delicate dissection to avoid catastrophic venous or arterial injuries.

Ultimately, the jejunum can be completely transected (at the site of the previous partial transection) using a laparoscopic stapling device.

This final step completes the dissection portion of the procedure, and the specimens, including the previously dissected gallbladder, can be safely removed using a laparoscopic endobag and extracted through the umbilical port site. Commonly, the fascial defect at the umbilical port sites needs to be enlarged to measure 3–4 cm; this defect is promptly sutured—following the extraction of the surgical specimen—and the Hassan trocar is reinserted through its original site prior to the reestablishment of the pneumoperitoneum.

20.3.2 Reconstruction Phase

The reconstruction commences with the creation of a duct-to-mucosa pancreaticojejunostomy. The free end of the jejunum is brought in close proximity to the pancreatic remnant in preparation for an end-to-side, duct-to-mucosa pancreaticojejunostomy. The anastomosis begins with the construction of the posterior anastomotic row, which is fashioned using a single-layered running 4.0 barbing suture; this eliminates the need for knots to secure suture lines therefore minimizing pancreatic manipulations (Fig. 20.6a, b). Then, a 2–3 mm jejunostomy is made to allow for a duct-to-mucosa anastomosis. After securing the pancreatic duct to the jejunal mucosa with a 5.0 synthetic nonabsorbable suture, the pancreatic duct stent is passed through the jejunal defect, and a duct-to-mucosa anastomosis is completed using, depending on duct size, five or six additional 5.0 synthetic nonabsorbable sutures in an interrupted fashion (Fig. 20.6c). Finally, a single-layered running anastomosis is performed using a barbed suture on the anterior side (Fig. 20.6d).

The completion of a pancreaticojejunostomy is followed by the creation of an end-to-side choledochojejunostomy. The previously transected CBD is gently dilated with the use of a laparoscopic Maryland dissector instrument (by gentle separation of the instrument jaws) to allow for an easier anastomosis. Then, a jejunostomy is performed on the antemesenteric portion of the free jejunal end with the use of a laparoscopic electrocautery; this site is again gently dilated with a laparoscopic Maryland dissector to approximately match the size of the previously transected choledocho.

An end-to-side duct-to-mucosa choledochojejunostomy anastomosis is performed using interrupted 4-0 synthetic absorbable sutures; the posterior row of the anastomosis is fashioned first and usually requires three to four interrupted sutures (Fig. 20.7a–d). Once the posterior row of the anastomosis is completed, a 6 to 8 French silicone tube (usually a pediatric feeding tube) can be customized to serve as a temporary biliary stent and inserted through the anterior opening of the choledochojejunostomy (Fig. 20.7e); this is followed by completion of the anterior row of the anastomosis in a similar fashion (Fig. 20.7f).

To minimize the tension of the choledochojejunostomy anastomosis, the authors routinely anchor the free end of the jejunal limb to the hilar plate using one or two interrupted 3-0 synthetic absorbable sutures.

In situations when the visualization of the transected bile duct is difficult, the authors use a looped suture around the base of a mobilized falciform ligament through a poke incision at the distal edge of the xiphoid to lift the liver cephalad (i.e., toward the abdominal wall); this allows for a wider working space and for an increased visualization of the transected bile duct, therefore, facilitating the construction of the choledochojejunostomy.

A jejunal loop is brought closer to the gastric remnant in preparation for an antecolic gastrojejunostomy; two 3-0 silk sutures are placed proximally and distally along the length of the future

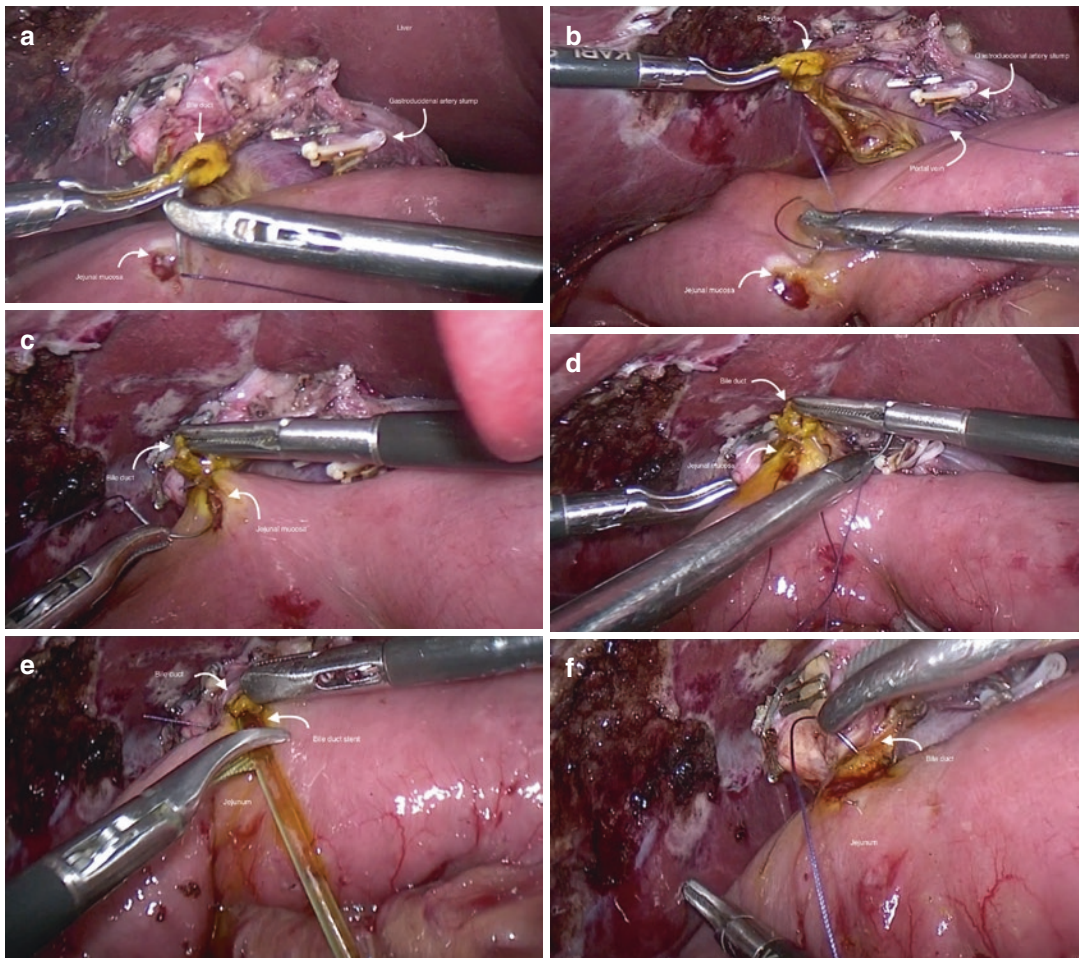

Fig. 20.7 End-to-side, duct-to-mucosa choledochojejunostomy construction: (**a-d**) posterior row, (**e**) placement of a 6 to 8 Fr silicone tube traversing the choledochojejunal anastomosis, (**f**) anterior row

anastomosis to serve as anchoring sutures so as to facilitate the alignment of the jejunal segment to the stomach remnant (Fig. 20.8a). The assistant can now hold the tail of the proximal anchoring suture up toward the abdominal wall while applying gentle tension to the distal jejunal limb; at the same time, the surgeon applies gentle cephalad tension to the stomach remnant; this maneuver stabilizes the gastrojejunal unit, and two enterotomies (a gastrotomy and a jejunostomy) can be easily created using an energy device.

A gastrojejunostomy is then completed using a stapling device (Fig. 20.8b); the resulting common enterotomy defect is closed with interrupted 3-0 silk sutures (Fig. 20.8c).

Finally, the abdomen is explored for evidence of bleeding, bile leakage, or remaining enterotomy defects; one surgical drain is placed posteriorly to the pancreaticojejunostomy (Fig. 20.9a) and one anterior to the choledochojejunostomy (Fig. 20.9b). The abdominal wall fascial defects are finally closed with the use of a Carter-Thomason needle suture passer.

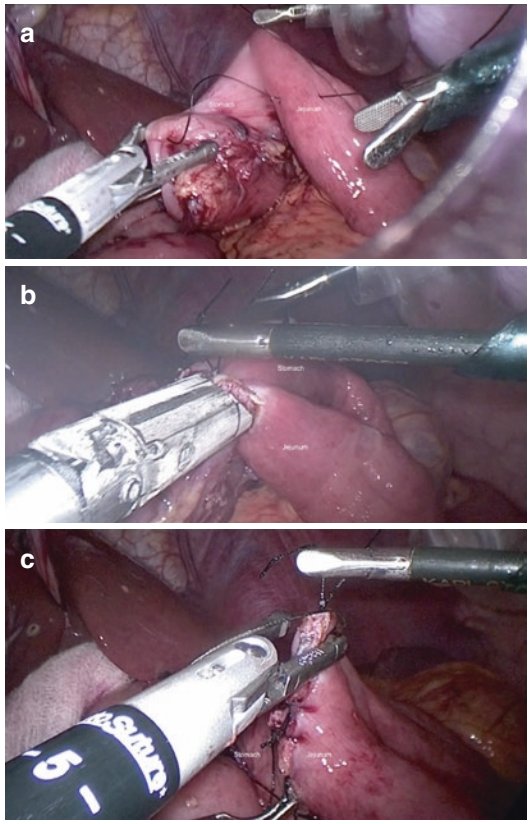

Fig. 20.8 Gastrojejunal anastomosis, (**a**) placement of two silk anchoring sutures to facilitate the alignment of the jejunal segment to the stomach remnant, (**b**) stapled gastrojejunostomy, (**c**) closure of the common enterotomy

20.4 Outcomes

Notwithstanding the undeniable interest of the international surgical community in pursuing minimally invasive techniques for pancreaticoduodenectomy, the overall benefit of this surgical approach remains a topic of debate and controversy.

Moreover, despite multiple case reports, case series, and retrospective cohort studies comparing MIPD to open pancreaticoduodenectomy—as stated earlier in this chapter—no randomized clinical trial exists comparing MIPD vs. OPD.

In an attempt to address the lack of level 1 data, several authors have conducted systematic reviews and meta-analysis of the available literature on MIPD [12–14].

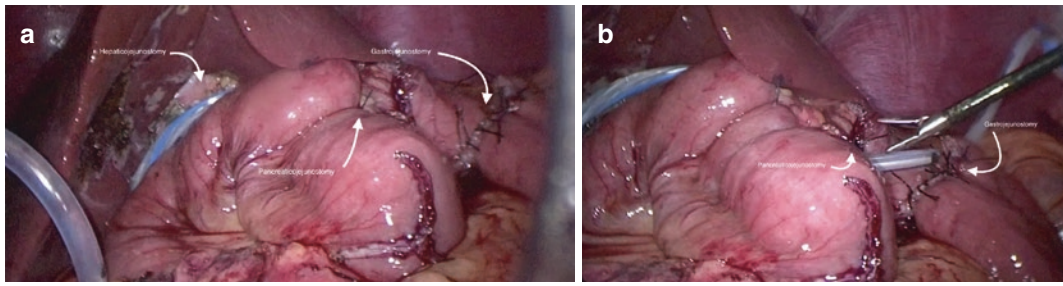

Fig. 20.9 Placement of trans abdominal surgical drains, (**a**) posterior to the pancreaticojejunostomy, (**b**) anterior to the choledochojejunostomy

The data emerging from these analyses share several common characteristics, and, in particular, the majority of published studies agree on the safety and feasibility of MIPD. Interesting results have been reported by Zhao et al.: the authors conducted a meta-analysis including 27 studies—from 9 countries in America, Europe, and Asia—with 2237 cases of MIPD and 11,854 cases of OPD. In their study, a subgroup analysis of laparoscopic pancreaticoduodenectomy (LPD) demonstrated that there were no significant differences between the two procedures (LPD vs. OPD) in terms of patient (i.e., age, sex, BMI, ASA) and tumor (i.e., tumor size and cancer diagnosis) preoperative characteristics, pancreatic postoperative fistula (grade B/C) rates, tumor size, reoperation, total cost, and 5-year survival rate. Furthermore, LPD was associated with decreased estimated blood loss (WMD [weight mean difference] = −341.61 mL, 95% CI = −578.57, −104.65 mL, P < 0.01), decreased delayed gastric emptying (OR [odds ratio] = 0.67, 95% CI = 0.49–0.90, P < 0.01), increased R0 resections (OR = 1.37, 95% CI = 1.11–1.67, P < 0.01), reduced length of hospital stay (WMD = −2.47 days, 95% CI = −3.77, −1.17 days, P < 0.01), and reduced postoperative cost but was associated with increased operative time (WMD = 60.25 minutes, 95% CI = 17.16–103.34 minutes, P < 0.01), significantly increased operative cost, and increased mortality (OR = 1.46, 95% CI = 1.15–1.85, P < 0.01) [13].

The results of this study must be critically reviewed, and in particular two of the findings deserve further discussion: (a) although the preoperative patient and tumor characteristics were similar, the majority of the analyzed studies lacked clear selection criteria for choosing MIPD vs. OPD, and it is reasonable to think that the most challenging cases were still performed via OPD; (b) the finding of increased mortality with MIPD appears troublesome; perhaps this is a function of the steep learning curve necessary to master this procedure, and it is directly correlated with the complications occurring during the initial learning phase [1].

Several authors have attempted to define a cutoff number of cases—during the learning phase—that would indicate proficiency with the technique; Baker et al. and Sharpe et al. suggested ten cases as a cutoff that resulted in resolution of the apparent increase in operative mortality [11, 15].

However, one must be cognizant that the time interval needed to achieve proficiency with this technique may be strongly influenced by preexistent familiarity with pancreatic procedures, dexterity with laparoscopic techniques, and hospital volume capable of providing a steady access to surgical cases amenable to MIPD.

In fact, as shown by Speicher and colleagues, a significant reduction in operative time approaching that of OPD can be observed after 10 cases; however it was not until 50 cases—over 3 years—that outcomes started to plateau [11]. Some of the most interesting results advocating for the use of MIPD over OPD were presented by Langan et al. and Croome et al. separately, as both authors suggested that MIPD was associated with a more rapid recovery compared to OPD which could lead to improved quality of life which may ultimately translate into earlier access to adjuvant systemic therapy [16, 17]. However, these findings remain to be corroborated by larger and more rigorous studies, and the debate between open versus minimally invasive pancreaticoduodenectomy is yet to be settled.

Conclusions

As the debate on the utility and perhaps superiority of MIPD vs. OPD carries on among academic circles, it is worth emphasizing that introducing a new MIPD program requires proper patient selection (e.g., small duodenal or ampullary lesions, small pancreatic lesions rather than large pancreatic masses with vascular involvement), especially in the steep first phase of the learning curve, a dedicated team (including surgeons, first assistant, and operating room nursing personnel), familiarity and proficiency with the open pancreaticoduodenectomy technique, and a baseline understanding that conversion to laparotomy may be necessary—particularly in the early learning phase—in order to avoid suboptimal outcomes.

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21 Laparoscopic Distal Pancreatectomy: How I Do It

Bergthor Björnsson and Per Sandström

21.1 Introduction

Laparoscopic distal pancreatectomy was first described in the mid-1990s, and in the beginning its evolution was slow, driven by enthusiasts within the field [1]. Initially this approach was found to be suitable for benign and premalignant lesions in the body and the tail of the pancreas. The advantages found compared to traditional open surgery are reduced blood loss, shortening of hospital stay, as well as higher proportion of spleen-preserving procedures [2, 3]. After the millennium, the application of this method in the case of pancreatic adenocarcinoma has increased. Although laparoscopic distal pancreatectomy has not yet been prospectively compared to its open counterpart, reviews of small series indicate that the new method is not inferior to the golden standard open surgery when it comes to oncological outcomes [4, 5].

The aim of this chapter is to describe a technique of laparoscopic distal pancreatectomy that can be applied in malignant lesions.

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21.2 Preoperative Workup

As pancreatic adenocarcinoma is often a rapidly progressing disease, the preoperative radiology should be done. In this regard a rule of no more than 4 weeks from radiology to operation may reduce the risk of unexpected findings during operation. A computed tomography of the pancreas, liver, and lungs or a magnetic resonance image of the pancreas and liver accompanied by computed tomography of the lungs should be considered minimum for preoperative staging.

The diagnosis of pancreatic adenocarcinoma can most often be strongly suspected from adequately performed radiological examination, and therefore histological verification is seldom needed for the decision to do a distal pancreatectomy. In cases were preoperative pathological diagnosis is needed, percutaneous biopsy should be avoided as this procedure is known to spread the disease [6]. Biopsy or fine needle aspiration with endoscopic ultrasound through the stomach may have a lower risk of tumor spread but should not be disregarded. We strongly advocate resection based on the radiological findings and refrain from any diagnostic biopsy in this setting.

Resectability for standard laparoscopic distal pancreatectomy is assessed by judging the distance of the tumor from the organs surrounding the pancreas (the stomach, left adrenal and kidney, proximal jejunum) and from the major vessels in the proximity (celiac trunk, left gastric

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artery, hepatic artery, superior mesenteric artery and vein, portal vein). In addition, the proximal part of the splenic artery should be free allowing for placement of clips as should the distal part of the splenic vein, allowing for the use of vascular stapler. Provided that no organ is involved and the major vessels do not have to be resected and the tumor does not reach the gastroduodenal artery, local resectability is present.

An additional information to look for in the preoperative radiology workup is the arterial and venous anatomy in the operation field. For instance, the drainage of the inferior mesenteric vein should be noted as a complete left-sided pancreatic resection may interfere with the vein.

Given that local resectability is present according to above and no sign of metastasis is found, the disease is deemed resectable with laparoscopic distal pancreatectomy and splenectomy.

Previous open surgery should not be considered contraindication for laparoscopic distal pancreatectomy although it may be wise to invest some additional time in the schedule of the procedure.

21.3 Preoperative Preparation

As with all laparoscopic procedures, the patient should be thoroughly informed about the risks of surgery, including the risk of conversion to open surgery. Anticoagulation prophylaxis should be started on the day before operation and continued postoperatively for 4 weeks [7]. The use of prophylactic antibiotics should be according to local routines and microbiology flora. When the surgery is planned in the outpatient's clinic, the patient is strongly recommended to stop smoking and keep up daily physical activities to reduce the risk of postoperative complications. Also, alcohol consumption should be evaluated and if in excess should be helped to reduce for the same reason.

21.4 Anesthesia

The patient is fasted at least 2 h before surgery. Intubation anesthesia with gas and muscle-relaxing agent is used. The patient receives a urinary catheter before surgery. Prophylactic medication against postoperative nausea and vomiting is given as indicated based on assessment by the anesthesiologist. We advocate intravenous patient-controlled analgesia (PCA) for control of postoperative pain, with morphine 1 mg/ml. This is used for the first two postoperative days, and thereafter paracetamol is often sufficient.

21.5 Patient Position and Trocars

The patient is placed in a supine position with the right arm at 90° from the body and the left arm along the side (Fig. 21.1). This allows for the operating surgeon and the first assisting surgeon to come close to the patient. While the supine position gives somewhat limited access to the tail of the pancreas and the spleen, placing the patient with the left side up limits the access to the right side of the pancreatic body. In order to improve the accessibility to the tail of the pancreas, the spleen, and the upper part of the greater curvature of the stomach, support is placed against the rib cage in the right axillary area as well as against the right hip. With these properly in place, the operation table can be tilted to the right allowing for better access to the abovementioned organ parts. Similarly support is placed under the patient's feet, and thereby reverse Trendelenburg position can be applied, further improving the access to the upper part of the greater curvature as well as the superior pole of the spleen.

The first trocar (10–15 mm) is placed directly above the umbilicus with open technique. As this trocar will be used for stapling the pancreas, it is important to use a trocar that allows the use of up to 15 mm stapler should this be needed. The second trocar (10–12 mm, used for camera) is placed laterally to the left rectus abdominis muscle in height with the umbilicus. Both the first trocars should be placed somewhat higher in the epigastric/right subcostal area if the patient is unusually tall as placing these around the umbilicus of tall patients will result in difficulties reaching the most cranial part of the dissection area and at the same time the angle for the dissection of the caudal border of the pancreas will be less than optimal.

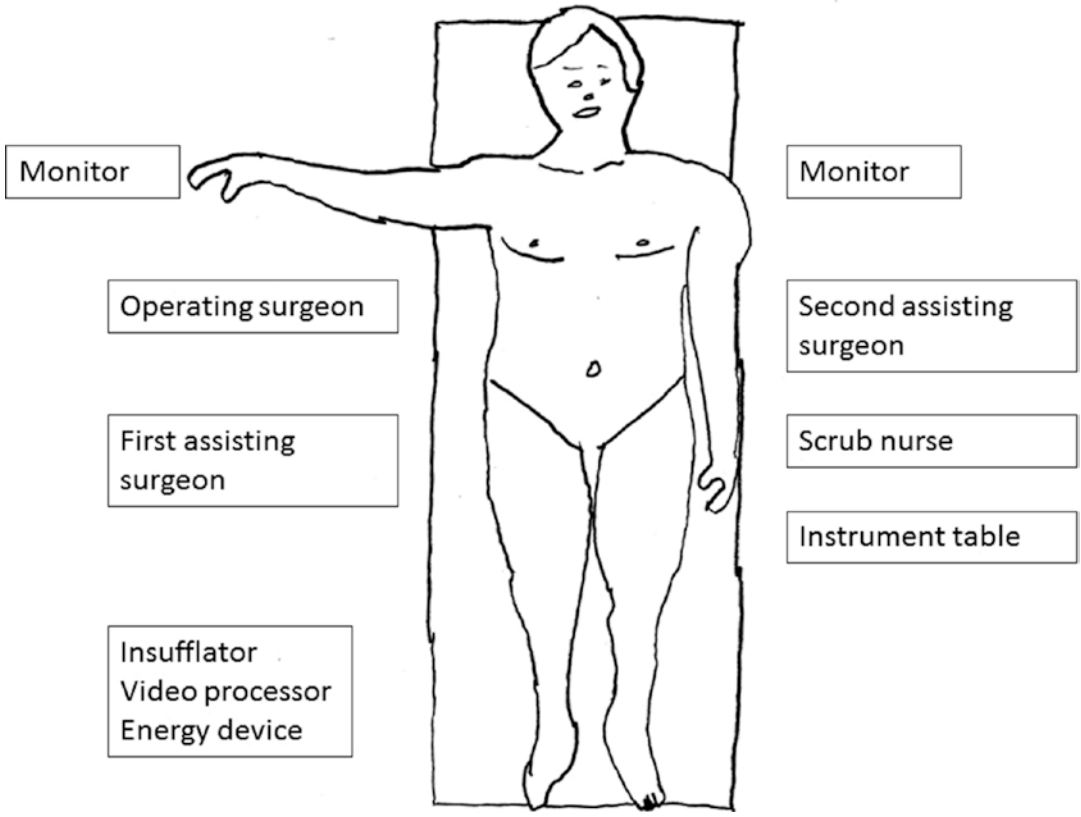

Fig. 21.1 Table and setup for laparoscopic operation of pancreatic body and tail

A 5 mm trocar is placed in the midline, in the epigastrium below the xiphoid process, and an additional 5 mm trocar beneath the ribs on the left side in anterior axillary line (Fig. 21.2).

21.6 Surgeons and Monitors

The main surgeon stands on the patient's right side cranially to the first assisting surgeon who steers the camera. The scrub nurse and the instrument table are on the patient's left side. Provided there is a second assisting surgeon, he or she is on the patient's left side, cranial to the scrub nurse (Fig. 21.1). Having a second assisting surgeon relieves the burden of working with instrument over the patient from the first assisting surgeon and allows for steering the camera with two hands that increases the quality of the camera work.

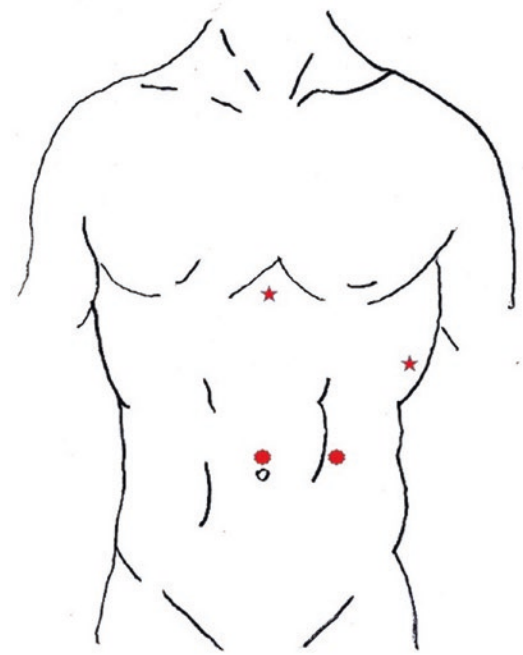

Fig. 21.2 Placement of ports for laparoscopic operation of pancreatic body and tail

Monitors are placed at the level of the patient's shoulder, on each side, and angled to fit the surgeons' need. When deciding the height of the monitors, care should be taken not to place these too high as this will result in non-ergonomic position of the surgeons. The video processor, gas insufflator, and energy for dissection instrument (see below) are placed on the patient's right side, caudally (Fig. 21.1).

21.7 Instruments

In addition to the trocars already mentioned, the following instruments should be included in the container: a forceps for the surgeon's non-dominant hand, where the existence of locking mechanism should be decided upon based on the surgeon's preference. This forceps will be used on both bowel and the pancreas and thus should be atraumatic. Forceps of the same type should be included for the assistant surgeon to use in the 5 mm trocar placed laterally on the left side; again, the use of locking mechanism should be decided upon by the surgeon using the instrument. A dissection instrument based on either bipolar energy, ultrasonic energy, or the combination of both is used with the leading surgeon's dominant hand throughout the operation. A right angle forceps should be available in order to facilitate dissection around vascular structures as well as the pancreas. A curved dissector may also be helpful for parts of the resection. A needle holder will be needed for the sutures placed on the stomach.

21.8 Laparoscopic Distal Pancreatectomy with Splenectomy: Step by Step

After gaining access to the abdominal cavity and inflation of carbon dioxide to 12 mmHg (15 may be used in case of obesity), the remaining trocars are placed under direct vision. With forceps and an energy device, any adhesions interfering with the surgical field are first divided. Next, the left colonic flexure, the proximal part of the descending colon, and the distal part of the transverse colon are mobilized. A gentle traction in medial direction will allow for the appearance of caudal part of the spleen.

The first step of the distal pancreatectomy is to mobilize the left colonic flexure and proximal part of the left colon. This is done by a medial traction of the colon allowing for the peritoneal fold laterally (white line of Toldt) to be visualized and opened. After mobilizing the colon, the superficial part of the splenocolic ligament is divided in order to avoid inadvertently damaging the spleen during the later steps of the resection (Fig. 21.3). The third step is to divide the gastrocolic ligament caudally to the gastroepiploic vessels. Care must be taken not to interfere with the colonic mesentery as there might be adhesions from the tumor or previous inflammation. This will provide access to the greater sack and the anterior aspect of the pancreas. This dissection typically starts on the right side of the antrum-corpus level and is extended cranially by also dividing the short gastric vessels until the left diaphragmatic crus is reached and the stomach has

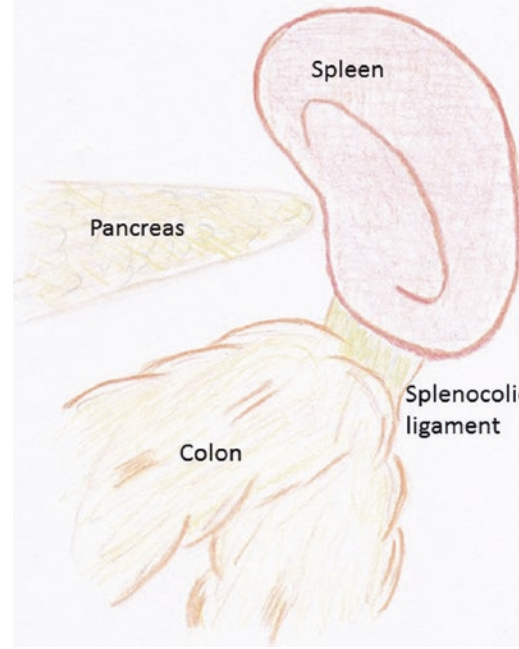

Fig. 21.3 The anatomic relationship between the pancreas, the spleen and the left colonic flexure

been completely separated from the spleen (Fig. 21.4). To the right side, the division of the gastrocolic ligament reaches the origin of the gastroepiploic vessels in order to allow for broad access to the pancreatic gland. After mobilization of the stomach, it is sutured against the anterior abdominal wall. This is done with monofilament suture, preferably size 2-0, on a straight needle. First the needle is inserted through the abdominal wall on the right side of the xiphoid process; when inside the abdominal cavity, the needle is passed through the posterior wall of the stomach and then through the abdominal wall again. By doing this, the stomach can be lifted anteriorly and cephalad, and the access to the celiac trunk as well as the superior border of the pancreas is improved.

The left gastric artery is now identified going from the celiac trunk in an anterior direction to the stomach. Following the left gastric artery in proximal direction, taking care not to injure the coronary vein will allow for the identification of the origin of the splenic artery and the hepatic artery. Lymph nodes along the common hepatic artery are dissected toward the celiac trunk and the origin of the splenic artery. After this the splenic artery is encircled with a rubber band. By initially following the left gastric artery and then doing the lymphadenectomy along the hepatic artery, the branches of the celiac trunk are securely identified. The dissection of the common hepatic artery lymph node exposes the portal vein at the cranial border of the pancreas. Depending on the angle, a curved dissector or right angle dissector will be needed to isolate the splenic artery. When the splenic artery has been isolated and encircled, the dissection behind the pancreas starts. Circulating the splenic artery before the dissection behind the pancreas adds safety in case of accidental injury to the splenic vein. However dissection of the splenic vein is easier to perform when filled than collapsed, and therefore the splenic artery should not be divided until the splenic vein has also been isolated. The transverse mesocolon is mobilized from the inferior border of the pancreas. Initially a curved dissector is used to lift the peritoneum, and an energy device is used to develop the plane of dissection. When the plane of dissection has been established, atraumatic forceps are used to apply gentle pressure, in cranial and anterior direction, to the pancreas, while the assisting surgeon pulls the transverse mesocolon in caudal and posterior direction. The direct branches to the splenic vein from the pancreas are divided with the energy device; no clips or ties are needed for this stage. In cases were the dissection plane between the pancreas and the splenic vein is hard to define, it may be helpful to initially dissect behind the splenic vein and around the pancreas that then can be anteriorly displaced while the splenic vein is released from the pancreas. When faced with a splenic vein that is difficult to detach from the pancreas, it should be remembered that dividing both structures at the same time is a safe option [8]. When the splenic vein has been isolated, the splenic artery is closed with locking clips and divided. After division of the splenic artery, the splenic vein may be divided although pancreatic division is preferably performed first in order to improve the access to the vein.

After division of the splenic artery, the dissection of the superior and posterior part of the pancreas is continued until a rubber band can be placed around it. The rubber band is then used to lift the gland, while a stapler is placed around it.

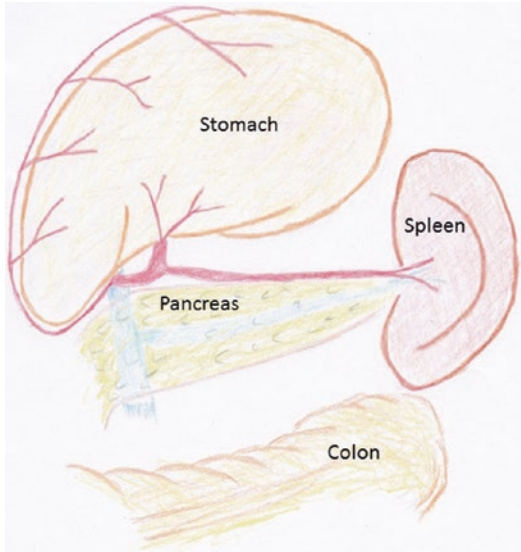

Fig. 21.4 The anatomic relationship between the stomach and the pancreas

There are some different staplers that can be used, and while none has been shown to be superior regarding the risk of postoperative pancreatic fistula, the stapler with the shortest/lowest possible stapler height should probably be used. When the stapler is placed around the pancreas, great care should be taken not to include the remaining branches of the celiac trunk in the stapling line, and this should be visually confirmed after the stapler has been closed but not fired. Firing the stapler is done slowly to compress the pancreatic tissue in order to reduce the risk of rupturing the gland along the stapler line. The use of reinforcement in the stapler line has not been shown to reduce the risk of postoperative pancreatic fistula.

After division of the pancreas, the splenic vein is stapled using vascular staplers. Care should be taken not to apply excessive lateral traction to the vein as this may result in tilting of the confluence against the superior mesenteric vein and subsequently narrowing it with the stapler. When the splenic vessels and the pancreas have been divided, the dissection is continued in an antegrade manner releasing the surgical specimen from the Gerota's fascia behind, making sure to follow the plane of the fascia and not to leave any lymphatic tissue behind. Should the preoperative radiology leave any doubt about involvement of the Gerota's fascia, the plane of dissection is kept behind the fascia in order to secure radicality of the posterior resection margin.

In cases were the inferior mesenteric vein drains to the splenic vein, care is taken to thoroughly close it with the energy device used for the dissection. As the dissection proceeds in distal direction, the deeper part of the splenocolic ligament is divided. When the dissection of the posterior border of the pancreas along with the splenic vein reaches the spleen, the splenorenal ligament is divided in caudo-cranial direction. In order to facilitate this, the operating table can be tilted to the patient's right side. The final step of the resection is to divide the cranial part of the splenorenal ligament. When the surgical specimen is free from the surroundings, a bag is introduced through the trocar above the umbilicus, and the specimen is placed in it. In cases with large tumors or splenomegaly, the bag may be introduced through a short Pfannenstiel incision in order to reduce postoperative pain. Before extracting the specimen, forceps are introduced through the 5 mm trocar in the epigastrium and through the 5 mm trocar subcostally on the left side. The subcostal trocar is removed, and a drain is pulled into the abdominal cavity with the forceps.

The drain is placed with its tip at the division line of the pancreas, and then the stomach is released from the stay suture. When the drain has been placed and secured to the skin, the incision cranially to the umbilicus (or a Pfannenstiel incision) is prolonged to allow for the extraction of the bag and the specimen. In order to optimize the work for the pathologist, the specimen is preferably sent fresh on ice. The larger incisions are closed with sutures in the fascia to reduce the risk of hernia formation.

The patient is taken to the recovery area for a few hours to see that there are no immediate complications. Drain amylase is evaluated on the first and third postoperative day; if elevated more than three times the upper limit, the drain should be kept until the leakage subsides.

21.9 Intraoperative Difficulties and Conversion to Open Distal Pancreatectomy

There are several situations that may call for conversion to open surgery. The major possible ones are bleeding, uncertain tumor margin or involvement of adjacent organs, and inability to dissect the whole circumference of the pancreatic gland at the site of division.

First of all patient safety should always be the first priority, and bleedings that can't be controlled laparoscopically may necessitate conversion. Before conversion for venous bleeding, increased abdominal pressure along with supplementary hemostatic agents may be used in order to control the bleeding. Venous bleeding can be at times substantially reduced if the splenic artery is closed. Should the situation still call for conversion pressure on the bleeding vessel either by

gauze or forceps will reduce blood loss during opening of the abdominal cavity.

Conversion because of advanced tumors needing additional organ or vascular resection may be needed, and the decision should be based on the particular surgeon's experience with advanced laparoscopy. Again, patient safety and the oncological adequacy of the operation are the key factors to consider. When faced with this situation, it may however facilitate the open part of the procedure to complete parts of the operation laparoscopically before conversion. This pertains especially to the division of the splenorenal ligament that is usually easier to perform laparoscopically than it is during open surgery.

Inability to safely dissect the whole circumference of the pancreatic gland may occasionally occur. Before converting to open surgery for this cause, lateral extension of the dissection at the inferior border of the pancreas may prove to be helpful, provided that this can be done without interfering with the tumor area. At times it may be difficult to isolate the splenic vein from the posterior aspect of the pancreas. Conversion only for this reason is however not needed as the splenic vein can be divided along with the pancreas [8].

21.10 Postoperative Care

Pain relief is obtained with patient-controlled analgesia for the first two postoperative days. In addition oral pain medication is supplied and continued for about 2 weeks postoperatively.

Mobilization is started at the recovery unit and continued at the ward. The patient is instructed to mobilize as much as possible directly after surgery, but heavy lifting is discouraged for the first six postoperative weeks. Per oral intake of liquids is encouraged already at the recovery unit and at the surgical ward, about 6 h after surgery intake of solid food is allowed.

Sick leave is granted for 2–4 weeks depending on the nature of work performed by the patient. Provided that the work does not include heavy physical duties, 2 weeks is found appropriate, while those with more physical demanding work may need longer recovery.

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22 Robotic-Assisted Pancreaticoduodenectomy: How We Do It

Ammar A. Javed, Aslam Ejaz, and Matthew J. Weiss

22.1 Introduction

Over the last two decades, improvements in surgical techniques and introduction of modern technology have led to the advent of minimally invasive surgery [1]. As such, laparoscopic and robotic approaches have been adopted for many routine abdominal procedures [1, 2]. Robotic surgery is now considered to be the primary approach for multiple general surgical, urological, and gynecological procedures. Due to the complexity of the operation, adoption of a robotic approach for pancreaticoduodenectomy (PD) has been slow [2]. This can be attributed to several reasons related to the complexity of the procedure including complex anatomy, the need for multiple complex anastomoses, sparse data on the impact on short- and long-term oncological outcomes, and the lack of training facilities [3–8]. However, some high-volume centers that are now performing robotic pancreaticoduodenectomy (RPD) have reported numerous potential benefits of using this approach including earlier postoperative oral intake, reduced operative blood loss, and decreased postoperative pain resulting in earlier recovery and shorter length of stay. A minimally invasive approach also potentially results in faster time to adjuvant therapy in patients with malignant disease.

The aim of the current chapter was to discuss patient selection, surgical techniques, and the current literature available on RPD.

22.2 Patient Selection and General Considerations

Given the technically challenging nature of RPD, patient selection is crucial. The extent of the disease should be evaluated using a pancreas protocol CT or MRI and serum CA 19-9 levels. If the pancreatic lesion is amenable to surgical resection, a preoperative assessment by an anesthesiologist is recommended. At our institute, RPD is performed for patients with benign, premalignant, and malignant lesions in the head and neck of the pancreas. As opposed to benign lesions, malignant tumors have the potential of vascular involvement requiring resection and reconstruction, which is technically challenging but possible when using a robotic approach. At smaller centers currently introducing RPD at their institute, it may be beneficial to initially perform this procedure in patients with benign or premalignant conditions until the learning curve has been achieved [9]. Furthermore, these centers should be cognizant of the fact that patients requiring multivisceral resections or those with large amounts of intra-abdominal adiposity may be

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poor candidates for RPD as in our experience the risk of conversion to an open procedure is high.

22.3 Surgical Technique

A comprehensive robotic surgical team is required to effectively perform RPDs including an anesthesiologist, nursing staff familiar with the robotic instruments and setup, an operating console surgeon, and a bedside surgical assistant for port placement, instrument exchange, and, perhaps most importantly, retraction and suctioning. Both the bedside scrub nurse and room circulator should be proficient at robotics to facilitate instrument setup and exchange.

Patients are positioned in a supine position with legs spread on a split-leg operating table and arms out at 90°. Peripheral intravenous access, an arterial monitoring line, and a Foley catheter are placed, and a nasogastric tube is inserted for decompression of the stomach. Monitors are placed over both the left and right shoulders of the patient to allow adequate view to the surgical assistants and scrub technician. The first assistant stands between the legs of the patients, while another assistant and the scrub nurse stand to the left of the patient. The abdomen is prepped and draped in the standard manner. The abdomen is then entered using either a Hasson or Veress technique and is insufflated to a pressure of 15 mmHg. A camera port is then placed in the supraumbilical position (12 mm), and the abdominal cavity is examined to rule out any iatrogenic injury as well as metastatic disease. If needed, an ultrasound of the liver can be performed to evaluate any metastatic disease in the liver. Subsequently two 8 mm ports each are placed in the right and left lower quadrant under direct visualization. Port placement is dependent on the type of robot being used, i.e., Si or Xi (da Vinci® Surgical Systems). At our institution, we commonly utilize the Xi robot (da Vinci® Surgical Systems), and the ports are placed in a straight line perpendicular to the midline. An accessory port (12 mm) can be placed in the right midclavicular line inferior to the robotic ports if needed. Once the ports have been placed, the robot is then docked from the patient side or over the head of the patient depending on the type of robotic system being used.

22.4 Exposure and Resection

Upon entering the abdomen, the hepatic flexure is carefully dissected, and the liver and gallbladder are pulled superiorly and cephalad to improve exposure. This is achieved by dissecting the ligamentum teres and encircling it using an Endoloop stitch. This is then suspended through the abdominal wall through a small stab incision in the subxiphoid area. A 3-0 prolene suture is placed around the infundibulum of the gallbladder in a figure-of-eight manner and similarly suspended through the abdominal wall at the right subcostal margin. The lesser sac is entered by dividing the gastrocolic ligament along the greater curvature of the stomach using a robotic vessel sealer (Fig. 22.1). This allows for adequate exposure of the anterior surface of the pancreas and is aided by superior retraction of the stomach by the third robotic arm. The neck and body of the pancreas are identified, and careful dissection is performed on the inferior margin of the pancreas until the superior mesenteric vein (SMV) can be visualized (Fig. 22.2).

Attention is then turned to the dissection of the porta hepatis. The common bile duct (CBD) is dissected and encircled with a vessel loop; care is taken to avoid injuring a replaced right hepatic artery if present. The right gastric artery is divided between clips. The common hepatic artery (CHA) is then identified, and the hepatic artery lymph node is removed which facilitates identification of the gastroduodenal artery (GDA) and the portal vein at the superior border of the pancreas. The GDA, proper hepatic artery (PHA), and CHA are carefully identified (Fig. 22.3). The GDA is test clamped to confirm adequate blood flow to the PHA via the CHA. In cases where the blood flow is potentially inadequate, a Doppler can be used to further confirm adequate hepatic blood flow. The GDA is then divided between Hem-o-Lok clips as well as a 2-0 silk tie. The CBD is then identified, and a Hem-o-Lok clip is

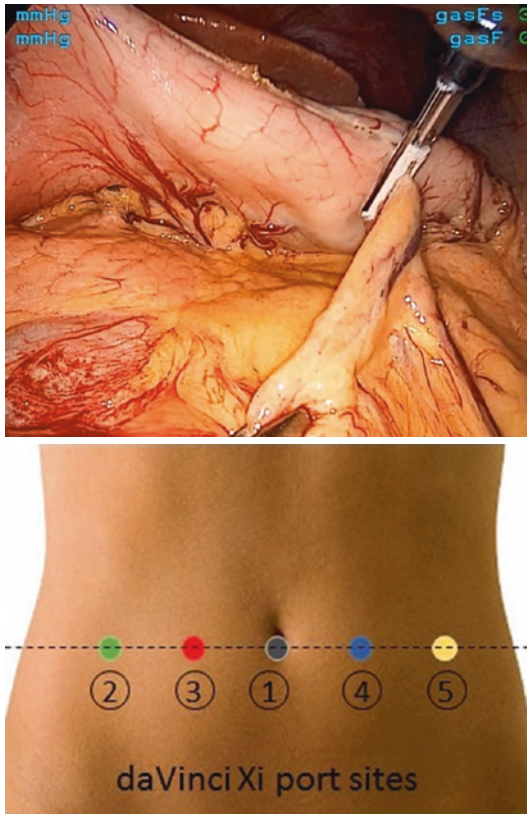

Fig. 22.1 Division of the gastrocolic ligament to enter the lesser sac

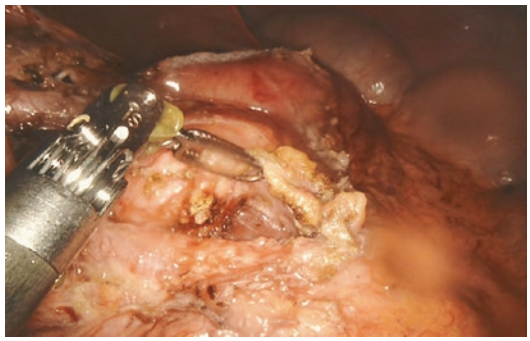

Fig. 22.2 Dissection at the inferior margin of the pancreas to identify the superior mesenteric vein and tunnel under the pancreas

then placed on the proximal margin of transection. This allows for dilation prior to reconstruction as well as prevents gross spillage of bile in the abdomen. The bile duct is then divided with electrocautery just below the Hem-o-Lok clip,

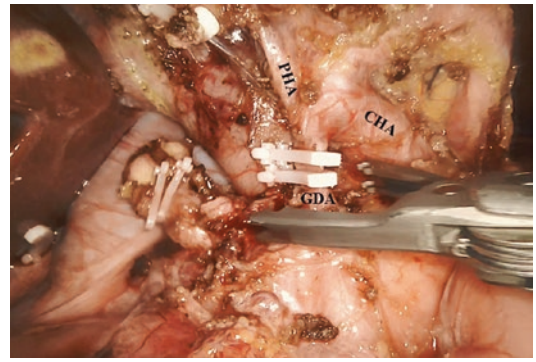

Fig. 22.3 Identification of common hepatic artery (CHA), proper hepatic artery (PHA), and gastroduodenal artery (GDA)

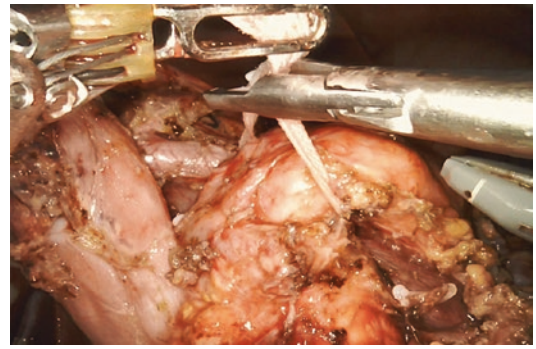

Fig. 22.4 Use of umbilical tape to suspend the pancreatic neck after completion of tunneling

and a portion is sent to pathology for frozen section. The stomach is then divided just proximal to the pylorus using an Endo GIA stapler after confirming that the nasogastric tube is not incorporated.

Attention is then turned toward the superior margin of the pancreas, and dissection is performed until the portal vein (PV) is identified. Subsequently, blunt tunneling is performed behind the neck of the pancreas and anterior to the PV in a cephalad direction. Prior to tunneling, the garstro-epiploic vein is identified and divided between two Hem-o-Lok clips. Once the tunnel is complete, an umbilical tape is looped around the neck of the pancreas and clamped using two Hem-o-Lok clips (Fig. 22.4). The umbilical tape around the pancreatic neck is then used to suspend the neck moving it in the superior-lateral direction, away from the PV, and a cautery is

used to divide the pancreas (Fig. 22.5). A separate pancreatic neck margin is cut and sent for frozen section. It is crucial to perform this division under direct visualization as the underlying PV/SMV/splenic vein complex is at high risk of injury. A Kocher maneuver is then performed and the duodenum is then dissected to just left of the aorta. The ligament of Treitz is sharply divided, and the first portion of the jejunum is then brought to the right upper quadrant and divided using the Endo GIA stapler. The mesentery of the small intestine is then divided using the vessel sealer device. At this point the Whipple specimen is left hanging from the uncinate process. The vessel sealer is used to carefully dissect the uncinate process off of the superior mesenteric artery in an inferior to superior direction (Fig. 22.6). Once the specimen has been completely extricated, it is placed in an EndoCatch bag and placed over the right side of the liver. The cystic duct and artery are then identified and divided between Hem-o-Lok clips, and the gallbladder is dissected off of the cystic plate with electrocautery. The gallbladder is placed in the EndoCatch bag with the Whipple specimen. The specimen is extracted either through an extension of the supraumbilical incision or through a separate Pfannenstiel incision.

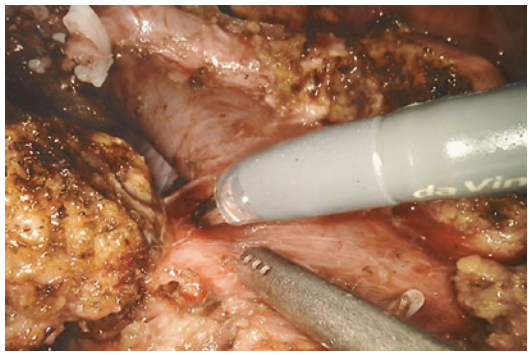

Fig. 22.5 Dissection of the pancreatic neck to expose the portal vein and superior mesenteric vein

Fig. 22.6 Dissection of the uncinate process from the superior mesenteric artery

22.5 Reconstruction

The reconstruction of the pancreaticojejunostomy (PJ), hepaticojejunostomy (HJ), and gastrojejunostomy (GJ) is performed in a similar manner as that in the open procedure in a counterclockwise fashion. The PJ is performed 2–3 cm away from the blind end of the jejunum. The posterior aspect of the pancreatic neck is sutured to the jejunal limb in a running fashion using a 3-0V-Loc™ suture (Fig. 22.7). Once this is complete, an enterotomy is made in the jejunal limb, and the main pancreatic duct (MPD) is identified for a duct-to-mucosa anastomosis. The duct-to-mucosa anastomosis is performed with simple interrupted suture (5-0 PDS). For smaller ducts, we frequently utilize a pediatric feeding tube as an internal stent (3-8 Fr). The number of sutures required for the duct-mucosa layer is dependent on the size of the MPD, but usually four to six stitches are adequate (Fig. 22.8). Finally, an anterior layer between the pancreatic neck and the jejunum is completed using a separate 3-0V-Loc™ suture in a running fashion (Fig. 22.9). In cases where the MPD is too small to be visualized or a pediatric feeding tube cannot be introduced, an invagination PJ can be performed.

Following the completion of the PJ anastomosis, the HJ is then performed. A small enterotomy is made in the jejunal limb, as far distally from the PJ as possible without creating redundancy in the bowel. Given that a Hem-o-Lok clip is placed on the CBD earlier in the procedure prior to division, considerable dilation of the duct is achieved, thus making it easier to perform the HJ anastomosis. The

Hem-o-Lok clip is removed, and approximately eight to ten interrupted sutures (5-0 PDS) (posterior row followed by anterior row) are placed between the bile duct and the jejunum to complete the HJ anastomosis in a duct-to-mucosa manner (Figs. 22.10 and 22.11). Of note this anastomosis should not be under any tension, and the number of sutures is dependent on the size of the hepatic duct.

The GJ anastomosis is then performed in an end-to-side manner in a hand-sewn fashion. A 3-0 V-Loc™ suture is placed between the distal stapled end of the stomach and the antecolic jejunal limb in a running manner, 5–10 mm away and parallel to the staple line. Once the posterior layer is complete, an opening is made in the stomach by removing a segment of the staple line (4–5 cm). An enterotomy similar in length to the opening in the stomach is then made in the jejunal limb. The posterior wall of the stomach with mucosa is then sutured to the posterior wall of the enterotomy in a running manner using a 3-0V-Loc™ suture, taking care to assure mucosa-to-mucosa apposition. Similarly, the anterior layer of the GJ anastomosis is completed in a running fashion between the anterior wall of the stomach and the enterotomy. Finally, another 3-0V-Loc™ suture is placed to complete the second anterior

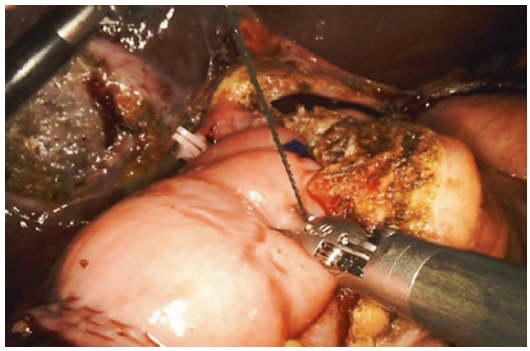

Fig. 22.7 Posterior layer of pancreaticojejunostomy

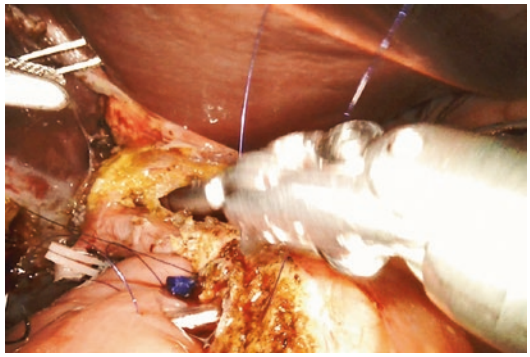

Fig. 22.8 Duct-to-mucosa anastomosis with stent placement

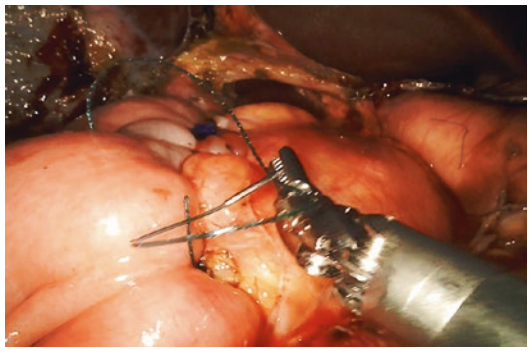

Fig. 22.9 Anterior layer of pancreaticojejunostomy

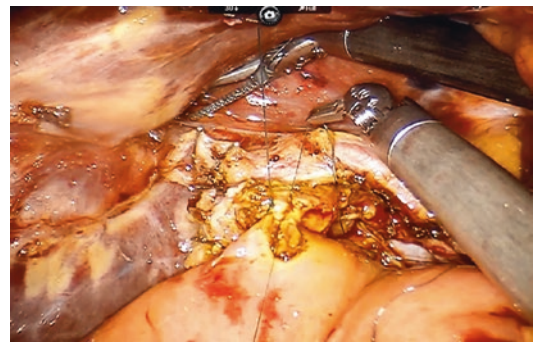

Fig. 22.10 Posterior layer of hepaticojejunostomy

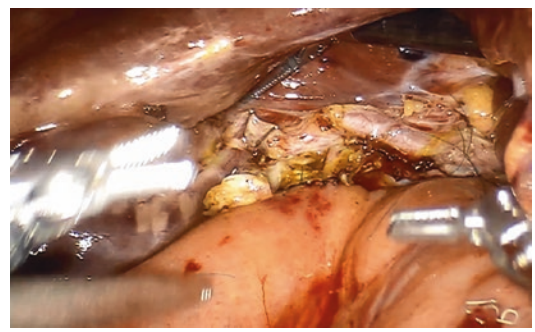

Fig. 22.11 Anterior layer of hepaticojejunostomy

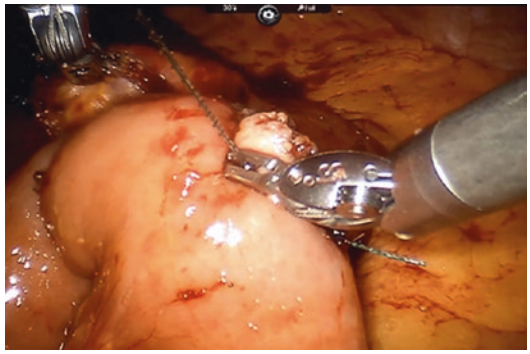

Fig. 22.12 Completion of gastrojejunostomy

layer of the GJ anastomosis (Fig. 22.12). Similarly, an Endo GIA-stapled anastomosis can be performed followed by a two-layer closure of the enterotomy site.

The abdomen is then thoroughly irrigated, and two drains are placed, anterior and posterior to the PJ anastomosis site, exiting through the lateral port sites. The EndoCatch bag is removed and all ports are removed under direct visualization. The abdomen is desufflated and the fascia used for port extraction is closed.

22.6 Current Literature on Outcomes of Robotic PD

Since the first human robotic surgery which was performed by Himpens et al., this approach has been adopted by multiple specialties [10]. Currently, many common procedures such as gastric bypass and Nissen fundoplication are frequently performed robotically. One of the first surgeons to report a robotic PD was Narula, who reported a case series of five patients who underwent a hybrid PD [11]. As compared to other abdominal procedures, the adaptation of RPD has still been slow due to the complexity of the operation, inherent instrument limitations, and the steep learning curve [2, 9, 11]. Initially, data on the benefits of a robotic approach was limited, but recent data from high-volume centers have shown favorable short- and long-term outcomes following PD [2, 12]. As there have been no level 1 randomized trials evaluating the impact of robotic vs. open PD, selection bias remains among the available literature. Furthermore, most case series and reports arise from high-volume centers and surgeons [1]. Despite this, appropriate patient selection is crucial for this complex procedure. In fact, some centers recommend that RPD should only be performed in patients with low-grade tumors with limited invasion and not those with pancreatic ductal adenocarcinoma (PDAC) [13, 14]. It is our experience and that of other centers, however, that RPD is an acceptable choice for patients with PDAC as well [15–20].

The technique of RPD still remains heterogeneous and is primarily dependent on the surgeon performing it. A hybrid approach can be utilized if it is felt that it would increase surgical safety, especially in cases where complex dissection around large vessels is required. Literature comparing hybrid and purely robotic approaches suggests no improvement in the operative time and outcomes based on the type of technique used [14]. Regardless of the type of RPD, an open pancreaticoduodenectomy (OPD) is associated with shorter operative time [6, 14]. Overcoming the learning curve and having a good team in the operating room have been identified as factors that can lead to a significant reduction in the length of these operations [21–24]. Furthermore, RPD is associated with a significant decrease in estimated blood loss and length of stay; however, the overall morbidity and mortality remain similar [1]. In a recent review by Wang et al., the rate of complications after a minimally invasive pancreaticoduodenectomy (MIS-PD) was found to range from 3.8% to 33.0%, which is comparable to that reported for open PD [1, 25, 26]. The most commonly reported complication was postoperative pancreatic fistula, and no decrease was observed in patients undergoing MIS-PD when compared to OPD [6]. These findings can however be confounded by both patient selection and the learning curve of RPD.

An important consideration when evaluating the efficacy of RPD is the rate of conversion to an open procedure. A recent review of current literature on minimally invasive PD by Wang et al. reported that the overall rate of conversion is

17.8%. Common reasons for conversion include tumor adherence, positive margin, unanticipated bleeding, and limited operative space [1, 14]. While conversion of RPD is considered by some to be an indicator to assess the quality of surgery, conversion should not be considered to be a failure of the procedure. It demonstrates the surgeon's keen judgment and can help avoid adverse outcomes.

In terms of oncological outcomes, Wang et al. reported the weighted average of resected lymph nodes to be 17.9, which according to existing literature on adequate lymphadenectomy is sufficient to provide optimal staging of disease [1, 27]. The reported rates of R0 resections for RPD ranged from 60% to 100%, which suggests that a RPD can help achieve similar oncological outcomes as compared to OPD [17, 20, 28, 29].

In conclusion RPD is increasingly becoming common and is a safe and feasible option for patients undergoing PD if performed by experienced surgeons at a high-volume center in a multidisciplinary setting.

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23 Enucleation and Transduodenal Surgical Ampullectomy for Pancreatic and Periampullary Neoplasms: How I Do It

J. Kaiser, P. Contin, and O. Strobel

23.1 Introduction

The formal anatomical pancreatic resections, partial pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy are the standard surgical procedures for malignant neoplasms of the pancreas. Nowadays these procedures are associated with low mortality but still with a considerable morbidity of up to 40% in high-volume centers [1, 2]. In addition standard pancreatic resections usually result in an important loss of normal pancreatic parenchyma with impairment of the exocrine and/or endocrine function of the pancreatic gland. In recent years there has been an increase in the diagnosis of benign neoplasms of the pancreas with the potential of progression to cancer [3, 4]. Many of these lesions are found incidentally during cross-sectional imaging for other purposes. Given the cumulative risk of malignant transformation over time, surgical resection may also be indicated for many of these incidental pancreatic lesions. However, given the high morbidity and the functional impairment after pancreatic resections and a lack of data on the true risk of malignancy in the natural history of theses tumors, there is an ongoing controversial debate on surgical resection versus observation of these lesions [5–7]. Together with other advances in pancreatic surgery, parenchyma sparing and less invasive types of pancreatic resections such as enucleation have been developed and increasingly used in recent years for benign and premalignant pancreatic tumors that do not require oncologically radical resections [8–11]. According to nonrandomized comparative studies and meta-analysis, these parenchyma-sparing procedures are associated with reduced severe morbidity and better long-term functional results if compared to standard resections [8, 11–13]. Several limited resections have been introduced for isolated or multiple pancreatic lesions. Two important parenchyma-sparing surgical procedures in pancreatic and duodenal surgery are enucleation for solid and cystic pancreatic tumors and transduodenal surgical ampullectomy for several diseases of the ampulla of Vater [8, 10, 11, 14].

23.2 Pancreatic Enucleation

23.2.1 Indications

Enucleation of pancreatic tumors can be a technically challenging intervention with high demands for preoperative diagnostics and perioperative management. Therefore, enucleations are mainly performed at high-volume

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centers experienced in pancreatic surgery [8, 9, 11, 15–17]. Enucleation involves shelling out the tumor without or with only minimal loss of surrounding normal pancreatic parenchyma. Enucleation has become a standard procedure for insulinoma and is by many considered a good option for other pancreatic neuroendocrine tumors [18, 19]. Others and we have shown that enucleation may also be the procedure of choice for small cystic pancreatic neoplasms such as branch-duct intraductal papillary mucinous neoplasms (BD-IPMN) without main pancreatic duct involvement [9, 11]. Enucleation is a good option for benign pancreatic lesions that do not involve the pancreatic duct. However, larger tumors located deep within the pancreas, especially in the pancreatic head, are less suitable for enucleation. Enucleation is not adequate for malignant tumors. With the advancement of minimally invasive techniques and instruments, laparoscopic and robotic enucleations are increasingly performed and appear to be safe [17].

23.2.2 Diagnostic Workup

For preoperative workup and exact localization of the tumor, computed tomography (CT) or magnetic resonance imaging (MRI) scans are routinely performed. Prior to operation of cystic pancreatic lesions, all patients should undergo MRI with MR cholangiopancreatography [20]. Endosonography can be of additional use if performed by the experienced endoscopist. This preoperative diagnostic workup should allow defining if a lesion is suitable for enucleation. However, despite modern cross-sectional imaging, the most important tool to decide on tumor enucleation versus formal resection remains the intraoperative experience of the surgeon during exploration [21–23]. Furthermore intraoperative ultrasonography might be useful for reconfirmation, even with successful preoperative localization of the tumor [24].

23.2.3 Open Enucleation: How We Do It

The most important steps of open enucleation for small nonmalignant pancreatic tumors are described below. The particularities to consider in enucleation of solid versus cystic lesions addressed were necessary. Many of the steps described here for open surgery may also be applicable in a minimally invasive approach.

Step 1: Access and exposure. A median laparotomy is best in patients without previous abdominal surgery. The abdominal cavity is examined for any abnormalities, and previously undetected metastatic disease is ruled out. Dependent on the location of the lesion within the pancreas, a focused exploration and exposure of the pancreas can be performed. To examine the entire pancreas, the exploration continues with opening of the lesser sac by dividing the gastrocolic ligament close to the transverse colon. The right colic flexure is mobilized to expose the head of the pancreas. Pancreatic head and duodenum are mobilized by Kocherization. For lesions in the body and tail, mobilization of the spleen and pancreatic tail may be necessary for precise assessment, particularly in obese patients.

Step 2: Localization of the lesion, assessment of the pancreas, and exposure for enucleation. Thorough assessment of the pancreas should include the exact localization of the lesion within the pancreas and the exclusion of additional lesions. Dependent on the superficial or deep location of the lesion, its localization is achieved by vision, palpation (transpancreatic palpation is facilitated by mobilization of the pancreas), and intraoperative ultrasound. In order to assess the possibility of safe enucleation, the exact localization of the tumor within the pancreas with a special focus on its relation to the pancreatic main duct (head, body, and tail) and additionally to the bile duct (head) has to be assessed. In case of doubt, intraoperative ultrasound is the best tool for this assessment. The portion of the pancreas

in which the tumor is located is further mobilized. In tumors of the body and tail, a plane is developed between pancreas and portal/splenic vein. It is helpful to use vessel tapes to lift up the segment of the pancreas containing the tumor and facilitates manipulation during the enucleation itself (Fig. 23.1). Dependent on the exact anatomy, it may be necessary to mobilize the splenic artery away from the superior border of the pancreas.

Step 3: Decision-making for enucleation. Enucleation is a good alternative for benign pancreatic tumors, but not adequate for malignant tumors. If the exploration reveals any signs suspicious for malignancy, these need to be addressed by further evaluation (e.g., by sending enlarged lymph nodes for evaluation by intraoperative frozen section). Enucleation is only feasible if the lesion does not directly involve the pancreatic main duct or the bile duct, as assessed by preoperative imaging and/or intraoperative ultrasound.

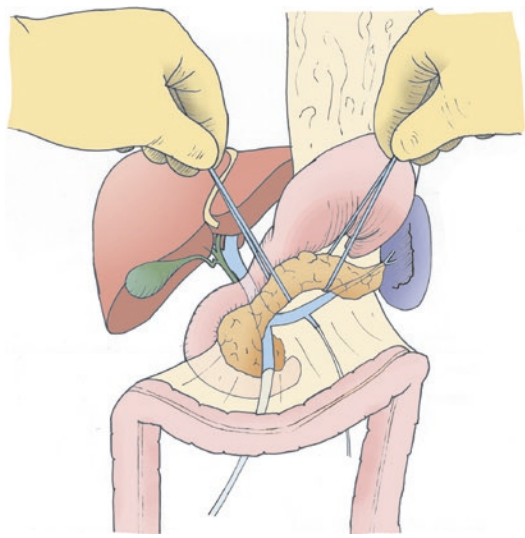

Fig. 23.1 Open enucleation, exposure for enucleation. Operative view after exploration and exposure for enucleation of a lesion in the pancreatic body/tail. The lesser sac was opened by separating the gastrocolic ligament. After localization of the lesion in the pancreatic body/tail, the pancreas is lifted up from the portal and splenic veins by two vessel loops placed on both sides of the tumor

While a location in the pancreatic body and tail and in the ventral aspect of the pancreatic head is ideal for enucleation, tumors located in the dorsal aspect of the pancreatic head and close to the mesopancreas/superior mesenteric artery are less suitable for enucleation. If the lesion is located far left in the pancreatic tail, a limited distal pancreatectomy may be a good alternative with comparable sparing of parenchyma. With the same rational lesions in the uncinate process may be addressed by uncinate process resection.

Step 4: Enucleation (sensu stricto). The enucleation itself should be performed by meticulous preferably blunt dissection and separation of the capsule/wall of the lesion and the surrounding pancreatic parenchyma. Enucleation should not be performed as removal of the lesion covered by a thin layer of normal parenchyma as this is not necessary for nonmalignant lesions but does increase trauma and risk of postoperative pancreatic fistula. The often thin parenchyma covering the lesion can be divided using a fine-tipped bipolar cautery. Once the lesion is exposed, mobilization continues by blunt dissection using closed small scissors or an endarterectomy spatula. For solid tumors such as pancreatic neuroendocrine neoplasms, a traction suture can be placed in the tumor to lift it up and allow exposure of the dissection plane (Fig. 23.2a). Cystic tumors (Fig. 23.2b) are more difficult to handle. Here, traction should be applied by blunt instruments carefully avoiding rupture of the cyst and spilling of the cyst content. Small feeding vessels can be addressed by small surgical clips or thin monofilament sutures. Bipolar coagulation may be used for superficial preparation but should be strictly avoided in the deep parts of the dissection plane to avoid a lesion of the ductal system. In solid tumors without relation to the ductal system, the dissection can be completed as described above (Fig. 23.3a). In contrast, in cystic lesions a communication with the ductal system has to be carefully assessed and addressed during the dissection. This is of utmost importance for enucle-

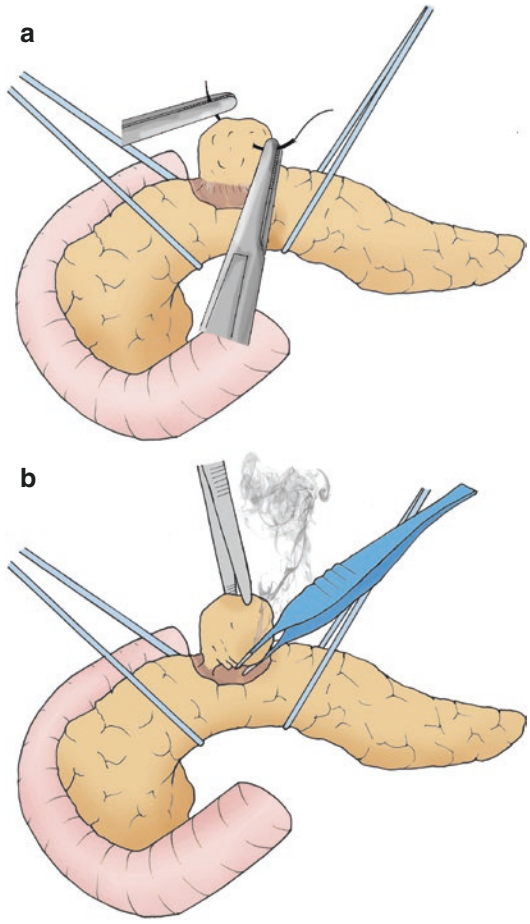

Fig. 23.2 Dissection during enucleation. (**a**) Enucleation of the solid tumor. A traction suture allows atraumatic handling of the lesion and exposure of the dissection plane during enucleation. (**b**) Enucleation of a branch-duct IPMN. Cystic lesions need to be handled carefully with blunt instruments avoiding leakage and rupture. The tumor is enucleated by careful separation of its capsule and the surrounding pancreatic parenchyma, preferentially by careful blunt dissection. Small vessels are divided between small surgical clips or monofilament stitches. Bipolar coagulation is used preferentially at the surface, but strictly avoided near the pancreatic duct

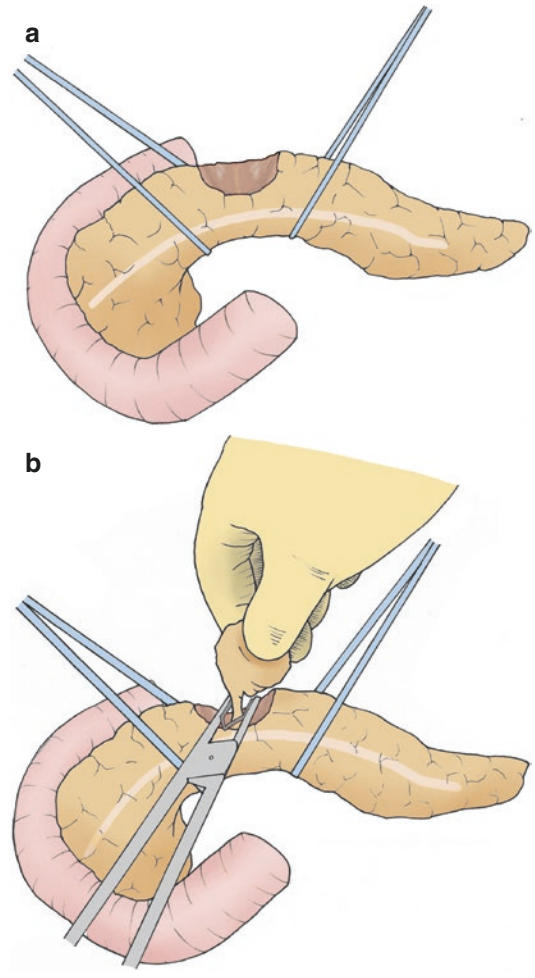

Fig. 23.3 Last steps of the dissection. (**a**) In solid tumors care has to be taken not to compromise the main duct during the last steps of dissection. (**b**) During enucleation of branch-duct IPMN, the connecting duct to the main duct has to be identified and to be specifically addressed. As last step of enucleation, the connecting duct is divided between surgical clips close to the main duct but avoiding compromising the main duct lumen

ation of branch-duct IPMN that are of course characterized by a communication to the main duct. This communicating branch duct has to be identified and is divided between small surgical clips (use two toward the main duct) close to the main duct but without compromising its lumen (Fig. 23.3b). Ideally the resection margin of the connecting duct is marked with a suture for specific evaluation by the pathologist.

As enucleation is not adequate for invasive lesions, immediate pathologic evaluation by intraoperative frozen section should be routinely performed, especially in suspected IPMN. When high-grade dysplasia or malignancy is found on frozen section, the operation should be converted to a formal pancreatic resection.

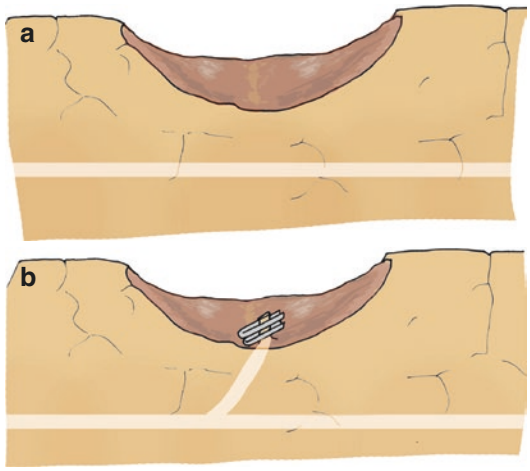

Fig. 23.4 Assessment of the enucleation site. Assessment for bleeding, major leaks, and integrity of the pancreatic main duct should be performed after any enucleation of solid (**a**) and cystic lesions (**b**). If in doubt, the integrity of the main pancreatic duct can be assessed by intraoperative ultrasound. After enucleation of branch-duct IPMN, the connecting duct should be identified and safely closed

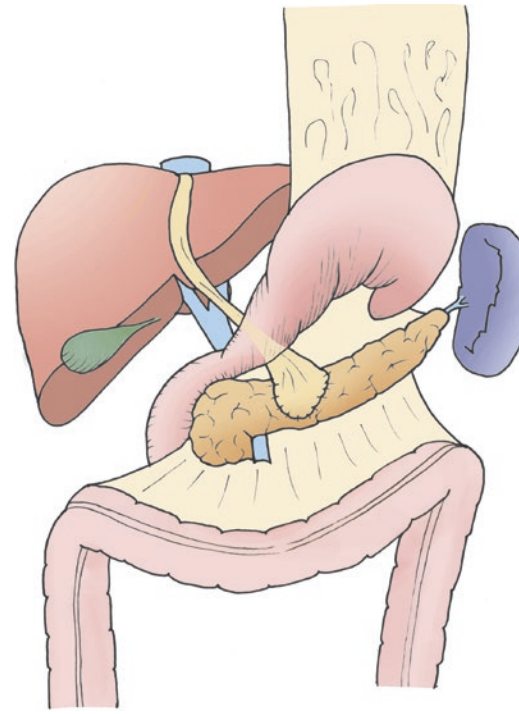

Fig. 23.5 Coverage of the enucleation site by serosal patch. The teres hepatic ligament flap is a good option for coverage of the enucleation site with a serosal patch

Step 5: Inspection of the enucleation site. Once enucleation is completed, the enucleation site should be carefully inspected for bleeding and a lesion of the ductal system. Some authors recommend secretin stimulation to identify major leaks, but this is not routinely used in our institution. Ultrasound can be very helpful to confirm integrity of the pancreatic main duct after enucleation (Fig. 23.4a). Identification and safe closure of the connecting ducts is crucial to prevent major leaks after enucleation of branch-duct IPMN (Fig. 23.4b). In case of a major leak or a lesion of the main duct, a conversion to formal resection is recommended.

Step 6: Suture, coverage, and drainage. Dependent on the location and size of the enucleation site, the resulting parenchymal effect can be addressed by coverage with a serosal patch and by parenchymal sutures or can be just left as it is. For coverage of enucleation sites in the pancreatic head, body, and proximal tail, a serosal patch using the teres hepatic ligament is a good option, similar to its use for coverage of the pancreatic remnant after distal pancreatectomy (Fig. 23.5) [25, 26]. In case of parenchymal sutures, any impairment of the main duct by compression or kinking has to be strictly avoided. For both parenchymal sutures and flap coverage, thin (5-0) monofilament sutures are used. There is no evidence for efficacy of any of the methods described above to reduce postoperative pancreatic fistula [10]. Soft passive drains are placed close to the enucleation site.

A clinical example of an enucleation performed for a small pancreatic neuroendocrine tumor is provided in Fig. 23.6. In our experience, enucleation for solid lesions is safe even if the lesion is located in direct vicinity to the pancreatic main duct. However, any coagulation or vessel-sealing device should be strictly avoided near the main duct. This may have implications for the decision for an open versus minimally invasive approach in the context of tumor localization. In Fig. 23.7 an example for enucleation of a large branch-duct IPMN is

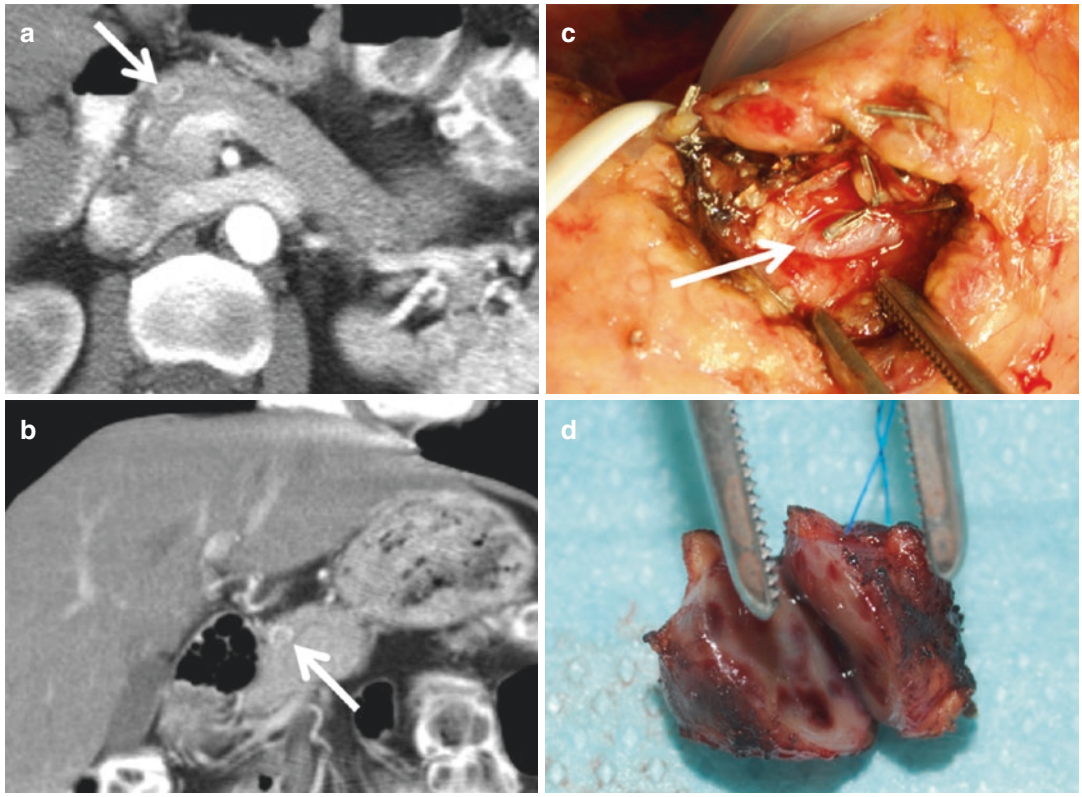

Fig. 23.6 Enucleation of a pancreatic neuroendocrine neoplasm (pNEN). (**a**, **b**) Preoperative contrast-enhanced computed tomography scan (arterial phase) in axial orientation (**a**) and coronary reconstruction (**b**) showing a hypervascular lesion (pNEN) in the pancreatic body (*arrow*) in direct vicinity to the main pancreatic duct. (**c**) Operative image after enucleation showing the enucleation site with the intact pancreatic main duct (*arrow*). Two vessel tapes are placed around the pancreatic body. (**d**) Enucleated small pNEN with typical appearance

provided. These lesions are often located superficially or even "exophytic" like in this case and are very suitable for enucleation. However, many lesions suspected to be branch-duct IPMN are indeed mixed-type IPMN extending to the main duct [27]. Therefore, high-quality preoperative imaging and thorough evaluation during the operation are important. In lesions with a wide connecting duct, an extension to the main duct has to be expected, and this can be addressed by frozen section. In tumors located in the uncinate process, an uncinate process resection can be a good parenchyma-sparing alternative, as highlighted in Fig. 23.8.

23.2.4 Postoperative Management

A fast-track regimen with mobilization as well as free fluid and solid food intake starting on the first day after enucleation is feasible and should be enforced. Postoperative laboratory tests on the first view postoperative days should include pancreatic amylase levels is serum and drainage outflow to detect the development of postoperative pancreatic fistula and pancreatitis as possible specific complications. Similar to standard resections, drains can be removed routinely on postoperative day 2 or 3, unless amylase or lipase values are increased or the appearance of drain fluid is suspicious.

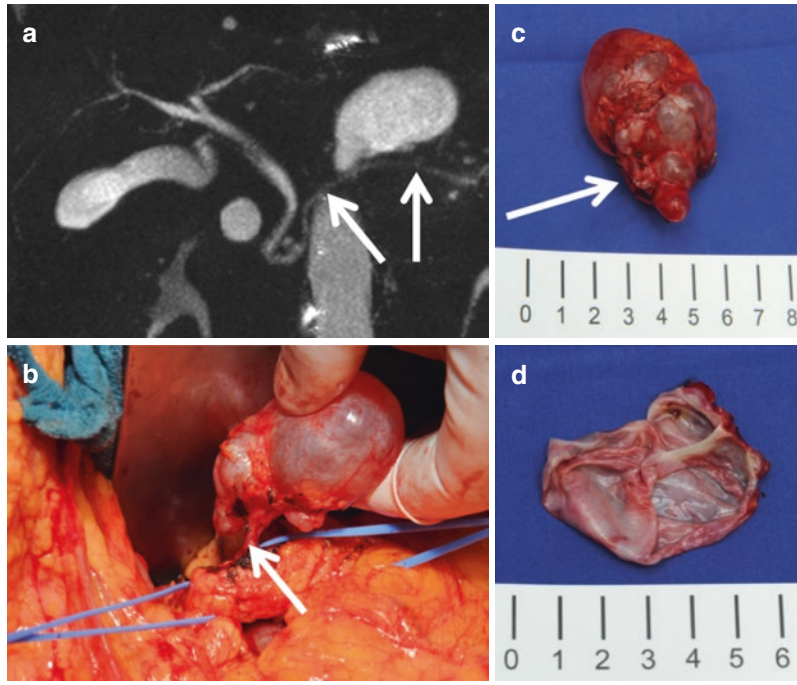

Fig. 23.7 Enucleation of a branch-duct intraductal papillary mucinous neoplasm (BD-IPMN). (**a**) Preoperative magnetic resonance cholangiopancreatography showing a 6 cm cystic lesion in the body of the pancreas without visible involvement of the non-dilated main pancreatic duct (*arrows*). The circular cystic lesion on the right side of the bile duct represents a superimposed renal cyst. (**b**) Operative image during enucleation. Two vessel loops are placed around the mobilized pancreatic body. The cystic lesion has been mobilized, and the small and non-dilated duct connecting the lesion with the main pancreatic duct (*arrow*) has been identified. The connecting duct can be divided close to the main duct between small surgical clips (not shown). (**c**) Enucleated BD-IPMN with centimeter scale. The *arrow* indicates the margin of the connecting duct with a clip. (**d**) Macroscopic appearance of the enucleated BD-IPMN after incision and opening reveals some mural thickening non-suspicious of malignancy. Histopathology confirmed BD-IPMN with moderate dysplasia

Enucleation differs from a formal pancreatic resection procedure (such as pancreaticoduodenectomy, distal pancreatectomy, or total pancreatectomy), which involves removal of a larger portion of the surrounding pancreas and tumor. The perioperative advantages of enucleation include a significantly shorter duration of the operation, reduced intraoperative blood loss, shorter intensive care and in-hospital stay, as well as lower rates of postoperative endocrine and exocrine pancreatic insufficiency [10, 11, 13]. However, as other pancreatic resections, enucleations are associated with a significant risk of postoperative complications, particularly postoperative pancreatic fistula [10]. The fact that pancreatic fistula occurs relatively often in patients that receive enucleation is not surprising because most patients with benign neoplasms have an otherwise healthy and, therefore, soft pancreas [28]. However, it has to be noted that that the majority of pancreatic fistulas after enucleations are clinically uncomplicated and the overall fistula rate is not significantly elevated when compared to formal pancreatic resections. In our own experience, the rate of clinically relevant pancreatic fistula is about 20% [10]. The development of postoperative pancreatic fistula has a larger impact on the

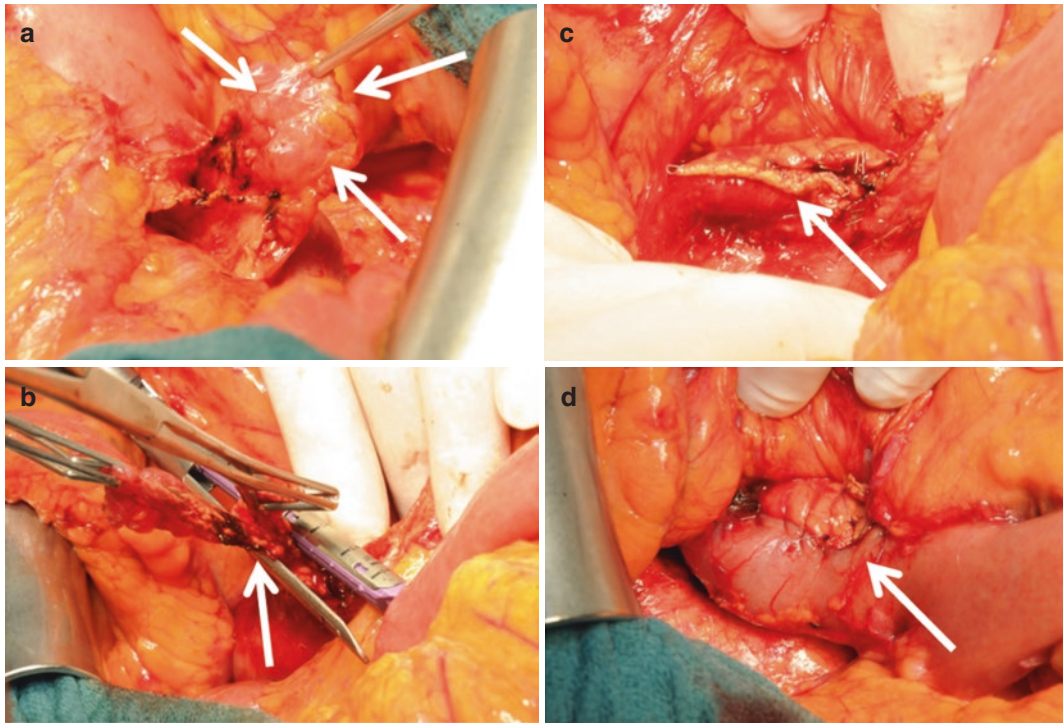

Fig. 23.8 Uncinate process resection for a branch-duct intraductal papillary mucinous neoplasm (BD-IPMN). (**a**) Operative view of the duodenojejunal flexure after partial mobilization of the suspected BD-IPMN originating from the uncinate process (*arrows*). At this location the resection can be performed as uncinate process resection including removal of the thin surrounding pancreatic parenchyma and reducing the risk of postoperative pancreatic fistula. (**b**) Operative view after further mobilization and placement of a lineal stapling device at the basis of the lesion (*arrow*). (**c**) Operative site with stapler line (*arrow*) after resection. (**d**) Operative site after additional coverage of the stapler line with duodenum (*arrow*)

postoperative course and recovery than after formal resections, because the overall surgical trauma after enucleation is considerably lesser and recovery in the absence of complications is faster. In meta-analysis, overall complications and rate of reoperations are comparable after pancreatic enucleation and formal pancreatic resection [13]. However, the most threatening complications associated with clinically relevant postoperative pancreatic fistula, i.e., postpancreatectomy hemorrhage (2.4%) and death (0.6%), appear to occur less frequently after enucleation [10]. One likely reason is that enucleation does not involve separation of larger vessels, thus reducing the risk of erosion bleeding from vessel stumps if compared to formal resections.

Follow-up examinations after enucleation depend on the disease-specific risk of recurrence and secondary tumors. After enucleation of IPMN, regular MRI scans every 6–12 months have to be recommended.

23.3 Transduodenal Surgical Ampullectomy

23.3.1 Indication

Transduodenal surgical ampullectomy is a surgical option for the management of benign tumors and stenosis of the major and minor duodenal papilla. Halsted first described it for a periampullary carcinoma in 1899 [29]. Today, this surgical procedure

has almost been forgotten and is not included in the clinical routine of many surgical centers. Due to technical advances and its minimal invasive approach, endoscopic ampullectomy is commonly considered as the first choice procedure for superficial benign ampullary neoplasms [30]. However, if endoscopic resection fails or recurrence of the ampullary neoplasm occurs, a surgical approach has to be considered. Transduodenal surgical ampullectomy is indicated for benign neoplasms that are located at or close to the ampulla [14]. Ampullary adenomas have to be resected with free margins either endoscopically or, if this is not possible, surgically, because they give rise to ampullary adenocarcinoma [31]. Furthermore, surgical ampullectomy can be a good treatment option for stenosis at the ampulla, for example, in the context of pancreas divisum [14, 32]. Compared to pancreatoduodenectomy, transduodenal surgical ampullectomy is a less invasive but very effective surgical procedure, which provides adequate oncological and superior functional clinical outcomes for benign and premalignant ampullary tumors [14, 33]. However, surgical ampullectomy is one of the technically most demanding procedures in duodenopancreatic surgery and requires meticulous technique for both resection and reconstruction.

23.3.2 Preoperative Diagnostic Workup

Preoperative endoscopy with use of a conventional side-viewing duodenoscope should be performed to detect ampullary lesions. Preoperative biopsy is mandatory. CT and MRI scans are performed in most cases but not mandatory in small lesions without signs of malignancy.

23.3.3 Transduodenal Surgical Ampullectomy: How We Do It

In the following the most important steps of transduodenal surgical ampullectomy for periampullary adenoma are described. Nowadays most periampullary adenomas are endoscopically removed, making surgical ampullectomy a rare procedure, reserved for experienced surgeons.

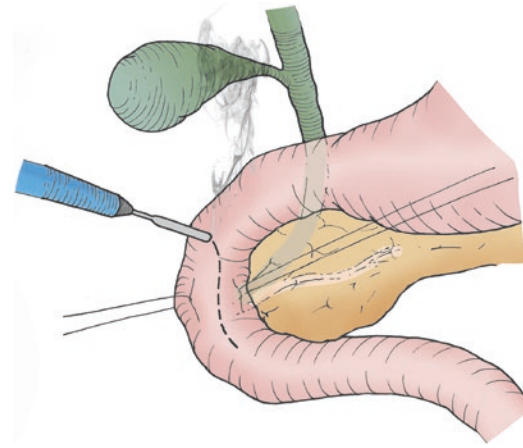

Fig. 23.9 Duodenotomy for surgical ampullectomy. Preparation for duodenotomy. After Kocherization tracking sutures are placed on both sides of the planned duodenotomy. Duodenotomy is performed in the anterolateral duodenum as slightly oblique incision

Step 1: Access and exposure. A median laparotomy or a right subcostal incision is preferable. The abdominal cavity is examined for any abnormalities, and previously undetected metastatic disease is ruled out. The hepatic flexure of the colon is mobilized inferiorly. The duodenum and pancreatic head are mobilized in a wide Kocher maneuver. In obese patients it can be necessary to mobilize up to the duodenojejunal flexure to enable adequate exposure.

Step 2: Localization of the ampulla. After Kocherization, the pancreatic head and posterior duodenum are assessed by palpation. The pancreatic head should be soft in most cases. Usually the ampulla can be localized by palpation. If not, a cholecystectomy is performed, and a probe or a Fogarty catheter is inserted antegrade via the cystic duct into the duodenum. Now, the exact location of the ampulla should be palpable.

Step 3: Duodenotomy. After localization of the ampulla, an adjusted longitudinal or slightly oblique anterolateral duodenotomy is made between traction sutures until the ampulla is nicely exposed (Fig. 23.9). Additional traction sutures improve exposure. Parasympatholytic

drugs like butylscopolamin are helpful to reduce peristalsis and enhance visibility during ampullectomy.

Step 4: Resection. Dependent on the size of the lesion and exposure, additional traction sutures (5-0 monofilament) can be placed to define the resection/circumcision line at the mucosal level aiming for a 5 mm free margin. We do not use saline/epinephrine injection to lift up the mucosa because this may impair exact anatomic reconstruction later. Local excision of the ampulla is performed by sharp dissection and bipolar coagulation or monopolar electrocautery with fine-tipped/needle point instruments in a meticulous technique. After dividing the mucosa, the muscularis/sphincter layer is reached, further mobilized, and finally divided. The previously inserted probe facilitates localization of the bile duct (Fig. 23.10). Usually, the bile duct is identified first and divided stepwise, while 5-0 or 6-0 absorbable monofilament sutures are placed in a stepwise manner. These tracking sutures serve to hold the duct in place and to prevent retraction and are used for adaptation with the duodenal mucosa during reconstruction later (leave the needles attached) (Fig. 23.11). After division of the bile duct, the pancreatic duct is identified just below and medial of the bile duct and handled in a similar stepwise manner using 6-0 or 7-0 absorbable monofilament sutures. If the pancreatic duct cannot be primarily identified, intravenous secretin administration may be used to stimulate pancreatic secretion. The extent and depth of the excision are defined during ampullectomy based on the tumor's size and depth.

The resected specimen is sent for frozen section evaluation. An intraoperative frozen section is mandatory to exclude malignancy requiring a pancreatoduodenectomy and to evaluate complete excision.

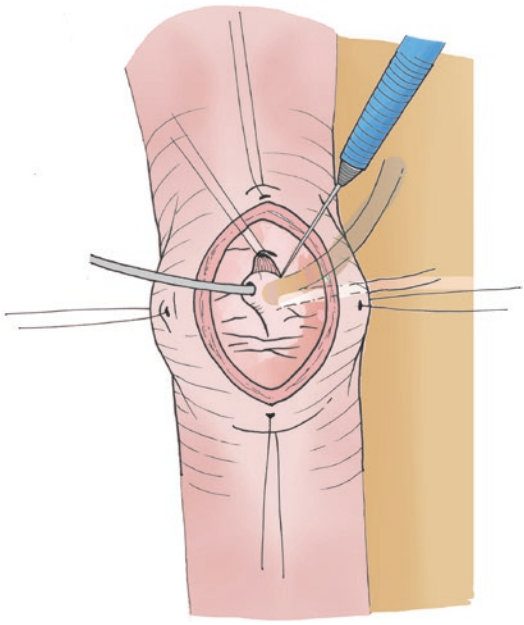

Fig. 23.10 Ampullectomy, mucosal incision. The ampullectomy starts with incision of the mucosa in the cranial aspect of the ampulla, where the bile duct is located. Additional tracking sutures can be used for the mucosa. The route of the bile duct is localized by a probe

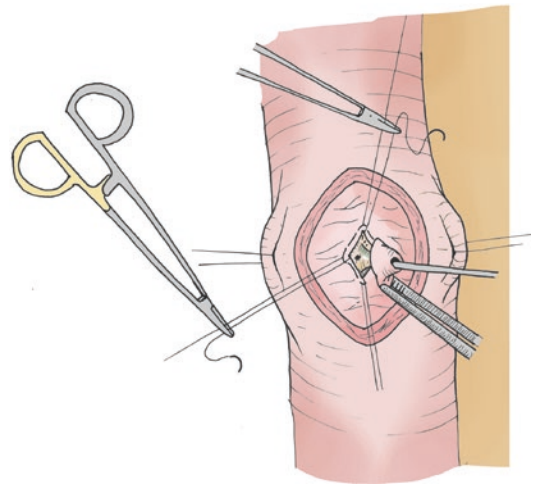

Fig. 23.11 Ampullectomy, transection of the ducts. The mucosa is divided, the ampulla mobilized. After division of the sphincter, only the bile duct and the pancreatic duct remain. The bile duct, which is larger and located cranially, is opened first. As soon as a duct is opened, fine traction sutures are placed in a stepwise manner to avoid retraction (not shown; see Fig. 23.6)

Step 5: Reconstruction. Except for very deep ampullectomies that are rarely indicated, the common bile duct and the pancreatic duct are usually implanted as common ostium. First a common ostium is created by interrupted sutures of the neighboring walls of common bile and pancreatic duct (6-0 monofilament) (Fig. 23.12). Thereafter, the sutures placed during resection are used to reimplant the common ostium by readaptation to the duodenal mucosa (duct-to-mucosa) (Fig. 23.13). Dependent on the size of the mucosal defect, additional sutures must be placed. All sutures are first placed; the adaptation and knot tying is performed as a separate step because the ducts will frequently not be visible any more after tying the knots of the duct-to-mucosa stitches. Assessment of patency of the ducts using probes is imperative.

Step 6: Closure. The duodenotomy is closed by a two-layered running suture (5-0 monofilament absorbable suture material). After closure a nasogastric tube is placed under digital control in the third part of the duodenum. Two soft passive drains are placed behind and in front of the duodenum. The cystic duct is closed. Some authors recommend insertion of a T-tube for bile diversion, but this can be safely omitted in our experience. The colonic flexure is repositioned and the abdominal wall closed.

Clinical examples of ampullectomies performed for a large ampullary adenoma and an adenoma with extension deep into the bile duct that could not be safely removed endoscopically are shown in Figs. 23.14 and 23.15, respectively. Technical feasibility of surgical ampullectomy is not defined by the overall size of the adenoma but by the diameter of its basis and by the depth of extension into the bile duct or pancreatic duct.

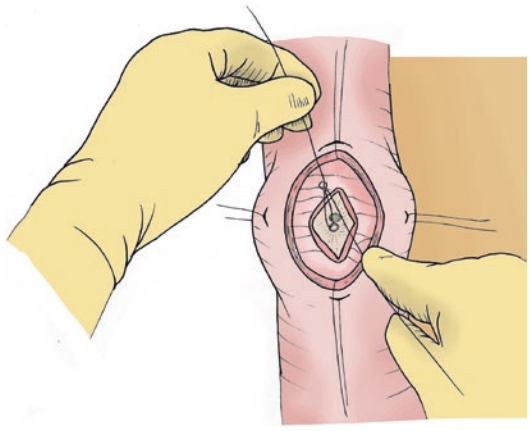

Fig. 23.12 Reconstruction: formation of a common ostium. The first step of reconstruction is the formation of a common ostium of bile and pancreatic duct by adapting sutures of their neighboring walls

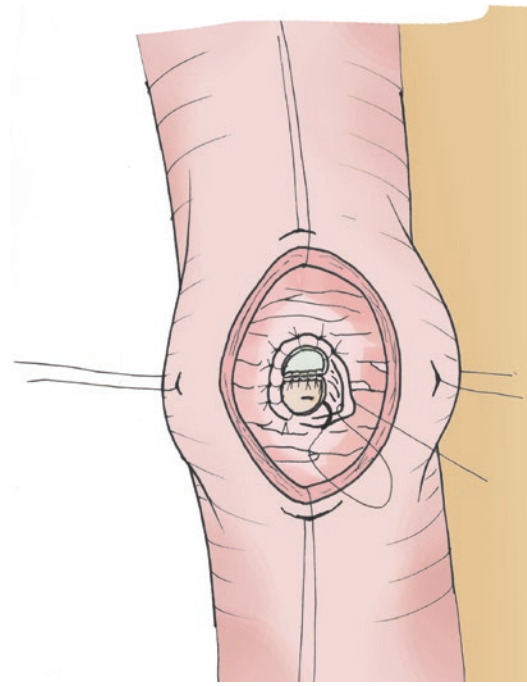

Fig. 23.13 Reconstruction: reinsertion. The common ostium is then reinserted by duct-to-mucosa stitches. For this purpose the ductal traction sutures placed during resection are reused (not shown). Additional sutures are placed dependent on the size of the mucosal defect. All stitches are first placed and tied later, to ensure visibility (see Fig. 23.6)

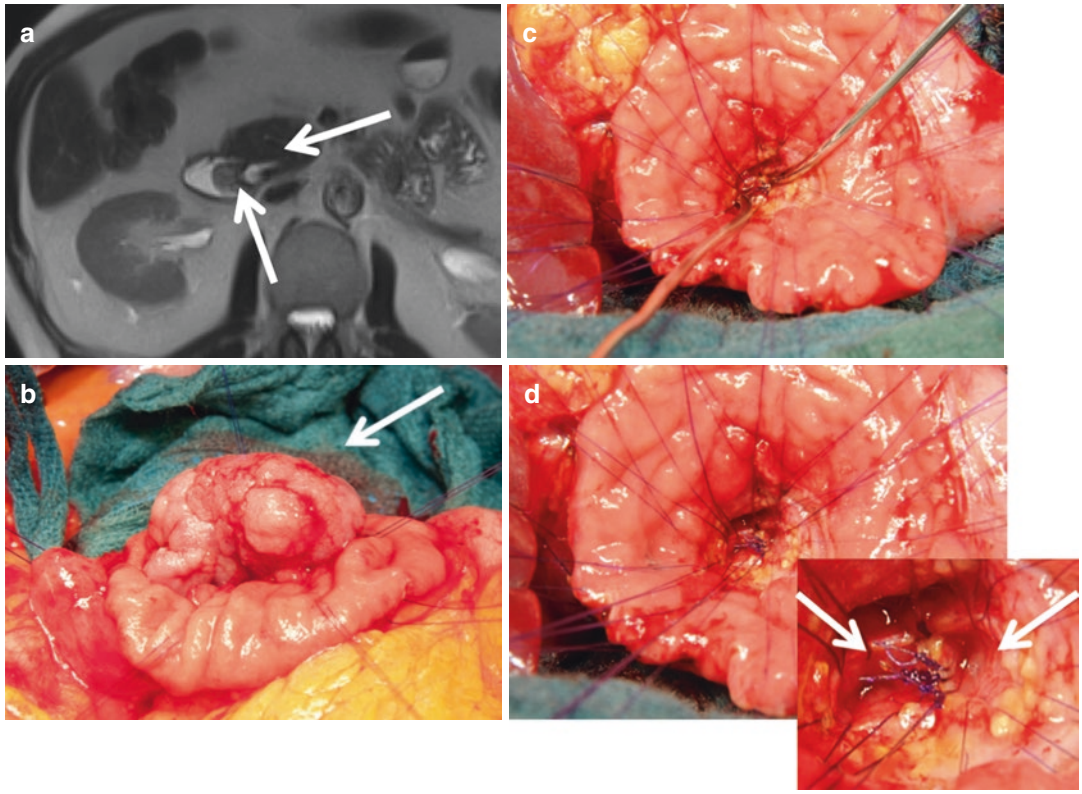

Fig. 23.14 Transduodenal surgical ampullectomy for a large ampullary adenoma. (**a**) Preoperative magnetic resonance imaging in axial orientation showing a large mass in the duodenum at the ampulla of Vater. The common bile duct and the pancreatic duct are dilated and visible close to the mass (*arrows*). (**b**) Operative view after mobilization of the duodenum, anterolateral duodenotomy, and placement of holding stitches. The large exophytic tumor at the ampulla is visible (*arrow*). (**c**) Operative view after resection of tumor and ampulla and placement of traction stitches for both common bile duct and main pancreatic duct (each with probe). (**d**) View without probes (*inset*: magnified view). The wall of bile duct and pancreatic duct are sewn together and will be reimplanted as a common ostium to the duodenal mucosa using the prearranged sutures placed during stepwise ampullectomy

23.3.4 Postoperative Management

The gastric tube is usually left for 2 and 3 days. Thereafter oral intake of liquids is started and gradually increased to solid food. Postoperative laboratory tests on the first view postoperative days should include pancreatic amylase levels in serum and drainage outflow to detect the development of postoperative pancreatic fistula and pancreatitis as possible specific complications. Increased levels of bilirubin are rare but indicate obstruction of the bile duct system. Drains can be removed routinely on postoperative day 2 or 3, unless amylase, lipase, or bilirubin levels are increased compared to normal serum value.

Transduodenal surgical ampullectomy is a feasible and safe surgical technique. Postoperative complications are comparable with the reported endoscopic morbidity rates. Procedure-related mortality is low (1.2%) and seems to be not higher compared to endoscopic ampullectomy, which ranges between 0% and 2% [14, 34].

Endoscopy with the use of a conventional side-viewing duodenoscope should be performed 6 months postoperatively to rule out recurrence of the disease.

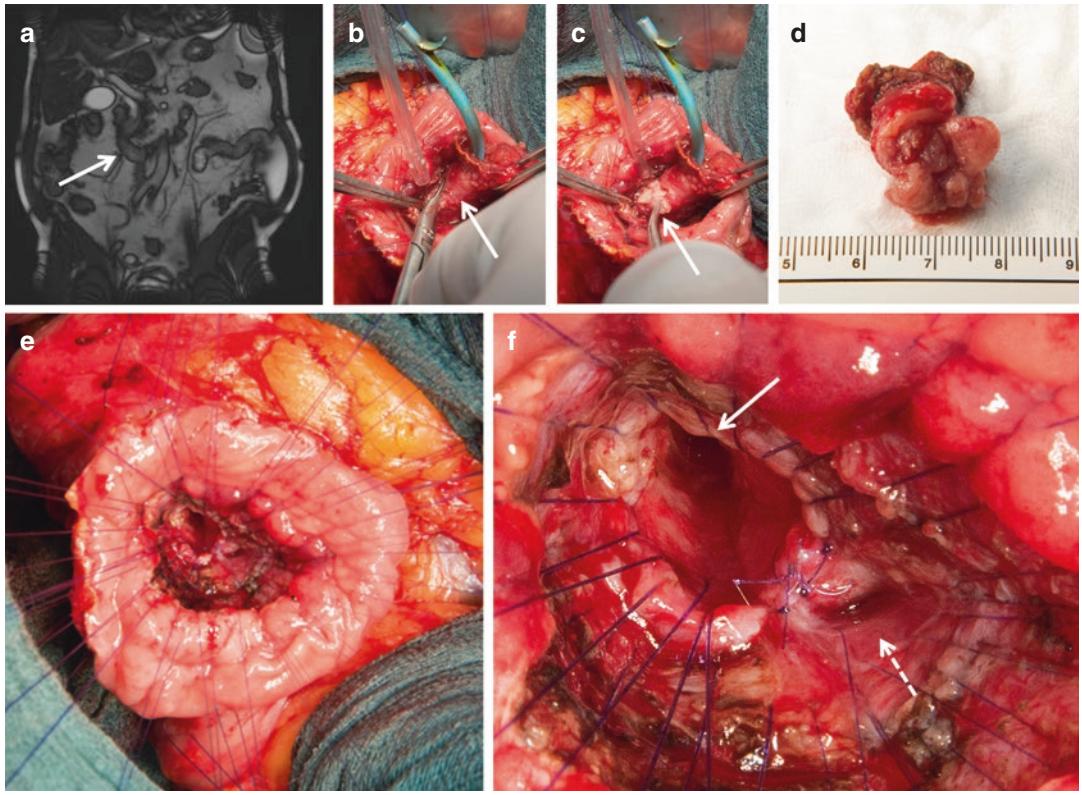

Fig. 23.15 Transduodenal surgical ampullectomy for an ampullary adenoma extending into the bile duct. (**a**) Preoperative magnetic resonance imaging (coronary reconstruction) showing a mass in the duodenum at the ampulla of Vater (*arrow*) and a dilated common bile duct. (**b**) Operative view after mobilization of the duodenum, anterolateral duodenotomy, placement of holding stitches, and mobilization of the ampulla. A biliary stent was left in place. *Arrow* indicating the bile duct. (**c**) After incision of the bile duct, the intraductal part of the adenoma is visible (*arrow*). (**d**) Resected specimen. (**e**) Overview with the prearranged duct-to-mucosa sutures before adaptation. (**f**) Magnified view of the common ostium formed of the common bile duct (*arrow*) and the pancreatic duct, in typical position at 4 o'clock of the bile duct (*interrupted arrow*)

Conclusions

Enucleation and transduodenal surgical ampullectomy can be performed with low morbidity and mortality rates in a high proportion of benign pancreatic neoplasms and ampullary pathologies, respectively. These procedures offer significant advantages with respect to both perioperative results and to long-term functional outcome when compared to formal pancreatic resection, such as pancreaticoduodenectomy, distal pancreatectomy, or total pancreatectomy and should belong to set of procedures of an experienced pancreatic surgeon. Procedure-specific limitations might occur due to size, localization, multilocularity, or main duct involvement and suspected malignancy or intraoperative frozen sections showing malignancy. For such cases the team needs to be always prepared for a conversion to more extended formal pancreatic resection. Thus, enucleation and ampullectomy represent effective parenchyma and function-preserving alternatives to the standard pancreatic resections for selected patients with benign pancreatic neoplasms with a risk for malignant transformation. While endo-

scopic treatment represents an important tool in patients with benign periampullary neoplasms, transduodenal surgical ampullectomy is a feasible and safe alternative surgical approach for the management of such lesions, especially after failure of endoscopic resection or in recurrent disease.

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24 Operative Complications and Their Management Following Resection for Pancreatic and Periampullary Cancers

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24.1 Introduction

Various forms of pancreatic resections are the standard operative approach for a variety of benign and malignant tumors of the pancreas and the periampullary region and remain the only curative treatment available [1, 2]. Pancreaticoduodenectomy (PD) is a complex surgical procedure, and with improvements in operative techniques and perioperative management of these patients, the associated mortality has decreased significantly from 30% to less than 5% [1, 3]. Despite these advancements the morbidity associated with PD remains high with the rates of postoperative complications ranging from 25% to 55% even at high-volume surgical centers [4]. A number of postoperative complications are associated with PD, postoperative pancreatic fistula (POPF) and delayed gastric emptying (DGE) being the most common ones. POPF and DGE combined can affect almost 50% of all patients undergoing PD [5]. Other major complications include surgical site infections (SSI), intra-abdominal abscesses leading to sepsis, and acute and delayed bleeding. These complications have great repercussions not only on the quality of life of patients but also lead to prolonged hospital stay and increased healthcare cost. Given that the morbidity associated with PD remains high, strong effort has been directed toward trying to find better ways to prevent and improve the management of these complications. The aim of this chapter was to review the current literature available on the four main complications associated with PD focusing on the prevention, diagnosis, and their management.

24.2 Postoperative Pancreatic Fistula

Postoperative pancreatic fistula (POPF) results from the leakage of pancreatic exocrine secretions from the site of pancreatic anastomosis. The reported rates of this complication range from 5% to 35% [1, 3, 6]. Multiple definitions have been proposed in the past to define POPF, and the definition proposed by the International Study Group on Pancreatic Fistula (ISGPF) in 2005 is the most widely used in literature. The ISGPF defines POPF as a drain amylase which is three times greater than the serum amylase levels at or beyond postoperative day 3 (POD3) (Table 24.1) [8]. The ISGPF definition further classifies POPF into three grades depending on the clinical impact of this complication and whether any changes in the management of the patient are required. A transient fistula, although has elevated drain

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Table 24.1 Grading of POPF as proposed by ISGPF

	Grade A	Grade B	Grade C
Clinical conditions	Well	Often well	Ill appearing/bad
Specific treatment[a]	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)[b]	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Signs of infection	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

Reproduced from Bassi et al. [7]
US ultrasonography, *CT* computed tomographic scan, *POPF* postoperative pancreatic fistula
[a]Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogues, and/or minimally invasive drainage
[b]With or without a drain in situ

amylase levels, results in no clinical symptoms warranting no changes in the management of the patient and is defined as a Grade A POPF. When POPF manifests with clinical symptoms and there is radiographic evidence of peripancreatic fluid collections, the pancreatic leak is categorized as a Grade B POPF. The management for Grade B POPF comprises of the use of antibiotics, placement of a postoperative percutaneous drainage, supplemental nutrition, or readmission to the hospital. The most severe form of pancreatic leakage is a Grade C POPF which consists of clinically unstable patients with sepsis and organ dysfunction and can result in death. Grade C POPF often requires reoperation.

Given the high prevalence of POPF and the associated clinical and economic impact, various methods have been described in the literature aimed at reducing the incidence of POPF. These methods include modifications in the surgical technique and postoperative management of these patients. Modifications in surgical techniques include variation in the type of anastomosis and application of biological and nonbiological agents to the site of anastomosis. Postoperative interventions include type and duration of drain placements, use of stents, the type of feeding, and the use of somatostatin analogues. Pancreaticojejunostomy (PJ) is a common method of reconstruction during PD. The conventional loop method of reconstruction is usually done either in an end-to-end or an end-to-side manner. However, the criticism regarding this technique is the activation of pancreatic enzymes due to exposure to gastric and biliary secretions which could potentially cause anastomotic breakdown. Several studies have compared conventional loop reconstruction to a Roux-en-Y reconstruction with isolated pancreatic drainage. In randomized control trials (RCTs) performed by Ke et al. and Tani et al., no significant difference was found in rates of POPF between the two methods [9, 10]. However, Ke et al. did report a reduction in the severity of POPF, shorter hospital stay, and reduced costs [9]. Nakeeb et al. compared the outcomes of isolated loop pancreaticojejunostomy with pancreaticogastrostomy (PG) and again found no significant difference in rates of POPF between the two groups [11]. However, this study did report a significant reduction in steatorrhea and early tolerance of enteral feeding in patients who underwent isolated loop pancreaticojejunostomy [11]. Pancreaticogastrostomy, although not as common, is another method of reconstruction that can be employed during a PD [11]. Multiple studies have looked at the rates of POPF between patients who underwent a pancreaticojejunostomy vs. a pancreaticogastrostomy (PG); however, the results have been conflicting [12–20]. Bassi et al.

in a prospective randomized study found no significant difference in rates of POPF between PJ and PG. Interestingly they found lower rates of multiple surgical complications, biliary fistula, DGE, and postoperative fluid collections in patients with PG. Similarly, other RCTs reported no significant difference in POPF rates between PJ and PG in patients who underwent PD [13, 19]. On the other hand, Figueras et al. in an RCT found significantly higher incidence and severity of POPF in patients who received PJ vs. PG after PD [15]. Another aspect of the surgical technique that has been studied is the method of reconstruction of the PJ anastomosis, i.e., duct-to-mucosa anastomosis vs. an invagination. Bassi et al. and Nakeeb et al. found no significant difference in the incidence of POPF between the two techniques [21, 22]. However, another RCT comparing duct-to-mucosa vs. invagination PJ reported a significant decrease in the incidence of POPF in patients who received an invagination PJ [23]. Furthermore, stent placement in the pancreatic duct during a duct-to-mucosa anastomosis in an effort to minimize the incidence of POPF has also been studied with conflicting results being reported. While several RCTs found no significant reduction in the rates of POPF in people who received stenting during PD as compared to those who did not, Poon et al. and Pessaux et al. reported significant reduction in the rate of POPF in patients who underwent pancreatic duct stenting [24–28]. Lastly, another method that has been employed to reduce the rate of POPF is the application of fibrin glue sealant at the site of pancreaticojejunostomy anastomosis. Lillemoe et al. found no significant difference in the rate of POPF between patients who received the fibrin glue application versus those who did not [29]. Similarly, another study found no significant reduction in POPF rates in patients who received temporary occlusion of their pancreatic ducts with fibrin glue as compared to those who did not [30].

Several postoperative approaches have been reported in literature to reduce rates of POPF. A prospective randomized trial by Bassi et al. reported a lower incidence of POPF in patients who received early drain removal on POD3 or sooner as compared to patients who had their drains removed on or beyond POD5. Moreover, there was a reduction in the rate of abdominal and pulmonary complications, shortened median hospital stay, and reduced hospital costs in patients with early drain removal [31]. Studies on the use of somatostatin analogues that inhibit pancreatic secretion have also been reported with conflicting results. Yeo et al. and Fernandez-Cruz et al. reported no significant difference in rates of POPF in patients who received octreotide [32, 33]. However, Allen et al. reported that that administration of pasireotide significantly reduced the incidence of Grade C POPF, pancreatic leak, and abscess formation [34].

Unfortunately, even after numerous attempts and various methods targeted toward reducing the incidence of POPF significantly, its rates remain high. Therefore, there is a dire need to continue research on techniques that can reduce the rate of this complication. Currently, the active clinical trials on POPF, as per ClinicalTrials.gov, involve studying (a) the use of ultrasound to predict the risk of POPF, (b) introduction of stents, (c) one-layer vs. two-layer duct-to-mucosa anastomosis, (d) reinforcement of staple line during distal pancreatectomy, (e) closed suction drainage vs. straight drainage, (f) early vs. late drain removal, (g) the use of prophylactic octreotide, (h) the use of hydrocortisone vs. pasireotide, and (i) standard vs. extended lymphadenectomy.

Patients experiencing POPF are in a catabolic state with an increased basal energy expenditure, which in addition to a high output fistula (>200 ml/day of exocrine secretion) leads to nutritional depletion and a disruption in the fluid electrolyte balance. Therefore, the management is mostly conservative if there is no peritonitis, bleeding, sepsis, or organ failure with a focus on restoring fluid and electrolyte balance, antibiotic administration, and providing adequate nutrition [35]. Although administration of total parenteral nutrition (TPN) is one way to provide nutritional support to the patient, it is associated with complications such as changes in gastrointestinal and pancreatic function and morphology and increased risk for wound infections and sepsis. Higher rates of fistula closure and earlier recov-

ery are seen with the administration of no or low-fat enteral nutrition. It reduces pancreatic secretions and therefore is a feasible alternative method to provide nutrition. Image-guided percutaneous or endoscopic drainage might be necessary in case of fluid collections around the pancreaticojejunostomy anastomosis site. Aspirated fluid is usually checked for amylase levels and cultured to guide the antibiotic treatment. Reoperation is only required in cases of refractory POPF, abdominal fluid collections that cannot be aspirated by interventional radiological techniques, organ perforation, sepsis, or hemorrhage from pseudoaneurysm [36].

24.3 Delayed Gastric Emptying

Delayed gastric emptying is the second most commonly reported complication after PD and was first reported by Warshaw et al., the reported incidence ranging between 14% and 61% [5, 37]. Although in most cases DGE is self-resolving, it causes substantial patient discomfort and can lead to prolonged hospital stay leading to increased healthcare costs [38]. The pathophysiology of DGE consists of various possible processes including trauma to the vagus nerve leading to gastroparesis or surgical removal of the duodenum that can affect the concentrations of motilin and pancreatic polypeptide leading to disruption in normal gastric motility [39–42]. The presence of preoperative diabetes and development of POPF and other complications are associated with development of DGE [43]. It is diagnosed when there is a significant output (>300 ml/day) from the nasogastric (NG) tube that is predominantly bilious in nature. Moreover, the patient is unable to tolerate solid diet on or beyond POD3. DGE has been classified into three grades by the International Study Group of Pancreatic Surgery (ISGPS) (Table 24.2). Grade A comprises of DGE requiring the use of nasogastric tube lasting longer than POD3, the reinsertion of nasogastric tube after POD3, or the inability to tolerate solid diet by POD7. Grade B DGE is defined as requirement of nasogastric intubation between POD8 and POD14, reinsertion of the nasogastric tube after POD7, or inability to tolerate solid diet by POD14. Grade C DGE includes nasogastric intubation requirement beyond POD14, the need to reinsert the nasogastric tube after POD14, or inability to take a solid diet by POD21 [44]. A CT scan is routinely performed to rule out an associated abscess or partial small bowel obstruction, and endoscopy can be performed to rule out any mechanical obstruction or edema at the anastomotic site.

Table 24.2 ISGPS classification of delayed gastric emptying

DGE grade	NGT required	Unable to tolerate solid oral intake by POD	Vomiting/ gastric distention
A	4–7 days or reinsertion >POD3	7	+/–
B	8–14 days or reinsertion >POD7	14	+
C	>14 days or reinsertion >POD14	21	+

DGE delayed gastric emptying, *NGT* nasogastric tube, *POD* postoperative day
Reproduced from Wente et al. [44]

Various technical modifications in the surgical technique have been employed with the intention to reduce the incidence of DGE. It has been postulated that preservation of the pylorus could lead to a decrease in the rate of DGE [4, 45, 46]. However, Tran et al. found no significant difference in the rate of incidence of DGE between patients who underwent a pylorus-preserving PD (PPPD) and those who underwent a standard PD [47].

The method of reconstruction of the duodenojejunostomy or gastrojejunostomy during PD has been widely studied and reported with the two common techniques including a retrocolic approach where the jejunal limb is brought through the right side of the transverse mesocolon or an antecolic approach involving its mobilization anterior to the transverse colon. Various clinical trials have reported conflicting results. Tani et al. reported a significantly higher incidence of DGE in patients who underwent a retro-

colic reconstruction as compared to antecolic reconstruction [48]. The duration of NG tube placement and hospital stay were also significantly shorter in the antecolic group, in addition to early tolerance of a solid diet. Similarly, Kurahara et al. reported a significantly higher incidence of DGE in patients with retrocolic reconstruction as compared to antecolic reconstruction [49]. The study also reported a higher incidence of Grade B and C DGE in patients who underwent retrocolic reconstruction. On the other hand, various trials have found no significant difference in DGE incidence between patients who underwent PD with an antecolic or a retrocolic reconstruction [5, 50, 51]. A meta-analysis including all studies comparing these two techniques reported antecolic reconstruction to be associated with a lower incidence of DGE [52].

In a study where radical PD along with extended retroperitoneal lymph node dissection was performed as compared with standard PD procedure, high rates of DGE were noted in the radical group, although this study was not statistically powered to assess the relative incidence of DGE [53].

Other surgical modifications that have been studied include type of anastomotic reconstruction, pylorus preservation, and subtotal stomach resection where only the pyloric ring is removed. A randomized multicenter study found no significant difference in the incidence of DGE, postoperative blood loss, length of operation and hospital stay, morbidity, and mortality between patients who underwent standard PD and those who underwent pylorus-preserving PD (PPPD). A meta-analysis, which included studies comparing subtotal stomach-preserving PD (SSPPD) with PPPD, concluded that SSPPD was associated with a lower incidence of DGE [54]. Preserving the left gastric vein, which may reduce the risk of ischemia around the pylorus ring, has been reported to be associated with a lower incidence of DGE. Similarly, a lower incidence of DGE has been reported in patients where a Braun enteroenterostomy was created. The rationale behind performing this enteroenterostomy is the reduction in the risk of kinking or edema formation at the site of anastomosis and directing the pancreatic and biliary secretions away from the stomach [55]. Moreover, Billroth-II reconstruction was found to be associated with a lower incidence of DGE and a significantly shorter hospital stay as compared to Roux-en-Y reconstruction for the gastrojejunostomy during subtotal stomach-preserving pancreaticoduodenectomy [56].

In addition to various surgical approaches, there have been various postoperative interventions to reduce DGE. Erythromycin is a macrolide antibiotic, which also is a motilin agonist [53]. A lower concentration of motilin has been proposed to cause gastric atony leading to DGE. Therefore, the use of erythromycin as a gastric motility agent has been studied. A significant reduction in the incidence of DGE was reported in a randomized controlled trial when patients were given intravenous erythromycin from POD3 till POD10 [53]. Similarly, another study reported a decrease in DGE, reduction in NG tube drainage, and early resumption of oral feeding with erythromycin [57]. Somatostatin and its analogues have also been used in an attempt to reduce complications after PD since they reduce pancreatic exocrine secretions. Prophylactic octreotide has been shown to have no effect on the rate of DGE [58]. On the other hand, somatostatin prophylaxis has been shown to increase the rates of DGE, increase the half-time of solid-phase emptying, cause a reduction in the fasting plasma motilin levels, and suppress plasma motilin levels for a prolonged period of time [59].

Currently, the active clinical trials on DGE, as per ClinicalTrials.gov, involve studying (a) antecolic vs. retrocolic gastro- or duodenojejunostomy, (b) conventional PPD vs. Roux-en-Y PPD, (c) the use of escalating temporary gastric electrical stimulation, (d) the use of prucalopride for gastroparesis, (e) the efficacy of VLY-686 (tradipitant) in relieving symptoms of gastroparesis, (f) Sancuso® for gastroparesis, and (g) gastric pacemaker implantation for gastroparesis.

Although DGE is a cause of significant patient discomfort, a majority of DGE is usually self-limiting. Therefore the management is conservative and includes gastric decompression through

nasogastric intubation, providing adequate nutritional support and ruling out a mechanical obstruction or edema of the gastrojejunostomy or duodenojejunostomy site. Moreover, one needs to be vigilant for other postoperative complications such as pancreatic leakage. As reduced levels of plasma motilin and motilin receptors have been considered to play a part in the development of DGE, motilin agonists such as erythromycin and metoclopramide may be used.

24.4 Surgical Site Infections (SSI)

Another commonly encountered postoperative complication after PD is surgical site infections. These are defined by the Centers for Disease Control and Prevention (CDC) as an infection that involves only the skin or subcutaneous tissue of a surgical incision occurring within 30 days after surgery [60]. It is usually associated with inflammation and pain [60]. The CDC has divided SSIs into three categories which consist of superficial incisional, deep incisional, and organ space SSIs. SSIs can require reopening of the wound leading to a delay in the initiation of adjuvant therapy, prolonged recovery and duration of hospital stay, and increased healthcare costs [61–64]. Intrinsic gut and skin flora are the contaminants in a majority of SSIs and include gram-negative bacilli, anaerobic bacteria, and gram-positive cocci, respectively. Since SSIs have great implications both in terms of patient recovery and healthcare costs, it is important to consider contributing risk factors and minimize the risk of infection. A retrospective study on patients who underwent PD found the length of surgery, main pancreatic duct thickness, and abdominal wall thickness to be significant risk factors for incisional SSIs. The risk factors for organ space SSIs included POPF, use of semi-closed drainage systems, body mass index more than 23.5 kg/m^2, main pancreatic duct diameter, and prolonged operative time [65]. Poor wound healing and increased dead space around the wound precipitated by hypoalbuminemia and a poor nutritional status also increase the risk of infection [66, 67]. Biliary drainage and stenting is often used in patients with jaundice. It is used to prevent cholangitis after endoscopic retrograde cholangiopancreatography or to prevent obstructive jaundice when there is a need for more time to better assess the patient or if a delay in surgery is expected [68]. Although initial studies reported results in favor of performing preoperative biliary drainage (PBD), a meta-analysis consisting of randomized controlled trials and comparative cohort studies reported no benefit of performing preoperative biliary drainage (PBD) in jaundiced patients and found PBD to be associated with an increased risk of overall postoperative complications as compared to surgery without PBD [69, 70]. A recent retrospective study that compared postoperative morbidity and mortality among patients who received biliary stents and those who did not reported no significant difference in overall postoperative surgical complications. However, they found biliary stenting, cardiac disease, and obesity to be significant risk factors for deep incisional SSIs [6]. Another study reported preoperative biliary drainage/stenting and receipt of neoadjuvant chemotherapy to be independent predictors for SSIs [70]. Moreover, blood transfusion has also been reported to be a risk factor for serious infections including SSI, bacteremia, and pneumonia after PD [71]. This can be attributed to suppression of T cell activity and inhibition of normal response by natural killer cells related to blood transfusions. Intraoperative bacterial contamination has been reported to adversely affect both the development of SSI and clinically relevant pancreatic fistula after PD [72]. Similarly prolonged operating time, contamination during surgery, poor surgical technique, and complications (such as bleeding, pancreatic leakage, and fistula) have also been identified as risk factors for SSIs [65]. Leakage of pancreatic secretions from anastomotic sites leads to a favorable environment for bacterial growth. Similarly, poor control of blood glucose, ineffective temperature regulation, and inadequate tissue oxygenation may all contribute to infection [73, 74].

Currently, the active clinical trials on wound complications, as per ClinicalTrials.gov, involve

studying (a) the use of wound protector, (b) the effect of high-dose insulin on infectious complication, (c) the use of wound VACs vs. standard closure, (d) procalcitonin as a predictor of early dehiscence after pancreatic surgery, and (e) the use of accelerated recovery pathway.

SSIs are diagnosed using clinical signs and symptoms such as erythema, pain, tenderness, warmth, drainage of purulent fluid from the site of incision, fever, abdominal discomfort, and difficulty in tolerating diet. In severe cases, signs of systemic sepsis might be present. A CT scan usually confirms any intra-abdominal fluid collections. Treatment modalities for SSIs include opening of the wound and, if systemic signs of infection are present, administration of antibiotics. Deeper tissues should also be inspected to rule out any infection. Dressing changes are sufficient for most patients to facilitate wound healing. Cultures of the pus from the wound site and drained collections of fluid/abscesses are used to guide the antibiotic therapy. For deep and organ space infections, percutaneous drainage combined with antibiotics is the treatment of choice. If the clinical status of the patient does not improve after percutaneous drainage and administration of antibiotics, a reoperation might be necessary.

The clinical status of the patient including hepatic and renal function, any associated allergies, and interactions with other medications are important considerations before administration of antibiotic therapy. The standard protocol for gastrointestinal surgery includes prophylactic intravenous administration of a bolus dose of first-generation cephalosporin immediately prior to incision, followed by 48 h of the same IV treatment [75].

24.5 Postpancreatectomy Hemorrhage

Although postpancreatectomy hemorrhage (PPH) is a relatively rare complication of PD with an incidence between 3% and 10%, it is associated with high mortality ranging between 20% and 50% [76]. Therefore, when it occurs it is a serious and potentially fatal complication. In 2007, the International Study Group for Pancreatic Surgery (ISGPS) proposed a universal definition and clinical classification of PPH [77]. PPH was divided into three categories (Grades A, B, and C) based on onset, location, severity, and its clinical impact (Table 24.3). The onset is either early, i.e., <24 h after the surgery, or late, i.e., occurring >24 h after the surgery. The site of bleeding can either be intraluminal or extraluminal. The severity of bleeding is graded as either mild or severe [77]. Mild PPH consists of small- or medium-volume blood loss, i.e., drop of <3 g/dl in the hemoglobin, and mild clinical symptoms which do not require reoperation or angiographic embolization. Severe PPH consists of a large vol-

Table 24.3 ISGPS classification for postpancreatectomy hemorrhage (PPH)

Grade	Time of onset, location, and severity of bleeding	Clinical presentation	Diagnostic flowchart	Therapeutic intervention
A	Early, intraluminal or extraluminal, mild	Unremarkable	Observation, hemoglobin measurement, US/CT	None
B	Early, intraluminal or extraluminal, severe Late, intraluminal or extraluminal, mild	Tachycardia, hypotension	Observation, hemoglobin measurement, US/CT, angiography, upper GI endoscopy	Fluid resuscitation, blood transfusion, optional follow-up in ICU, therapeutic endoscopy, vessel embolization, reoperation
C	Late, intraluminal or extraluminal, severe	Oliguria, hypovolemic shock	CT, angiography, upper GI endoscopy	Fluid resuscitation, blood transfusion, ICU hospitalization, bleeding localization, therapeutic endoscopy, vessel embolization, reoperation

US ultrasonography, *CT* computed tomographic scan, *ICU* intensive care unit
Reproduced from Wente et al. [77]

ume of blood loss, i.e., drop of >3 g/dl in the hemoglobin, and has significant clinical impairment which warrants invasive treatment [77]. Early PPH is usually iatrogenic or due to an underlying coagulopathy, arterial bleeding, or inadequate hemostasis, whereas late PPH is usually due to the development of pseudoaneurysms [78–84]. The leakage of exocrine pancreatic secretions and enzymes leading to erosion of peripancreatic blood vessels, arterial iatrogenic injury leading to a pseudoaneurysm, and ulceration at the gastrojejunostomy anastomotic site are other factors that contribute to late PPH [77]. Patients with pancreatic leak, clinical signs of infection, and bile drainage are at high risk of developing PPH [78, 85, 86]. Moreover, male sex, vascular resection, very low hospital volume (≤7 pancreaticoduodenectomies per year), and postoperative intra-abdominal/wound infection have been reported to be independent predictors for developing PPH during the index visit [87].

Great vigilance and monitoring of clinical signs is required in the postoperative period to diagnose PPH. Patients can develop symptoms consistent with blood loss such as tachycardia and hypotension. In case of massive blood loss, the patient can develop hypovolemic shock. Blood can be observed in the nasogastric tube, abdominal drains, vomit, or stool. Sentinel bleeding which includes small quantities of blood loss can sometimes precede an episode of massive blood loss [78]. With a reported rate of 46% in patients who develop PPH due to pseudoaneurysms, sentinel bleeding should be diagnosed early and taken seriously [88]. Apart from clinical signs and symptoms, a drop in the hemoglobin levels can also indicate PPH. Imaging studies such as upper GI endoscopy, scintigraphy, CT, and angiography can be used to confirm PPH. The onset and severity of PPH guide the therapeutic interventions required for management of these patients. Grade A PPH that includes early/mild cases usually just requires close monitoring and no major deviation from the routine postoperative management. Grade B PPH that includes early/severe and late/mild cases usually requires diagnostic and therapeutic interventions. The patient is stabilized clinically by volume resuscitation and blood transfusions. Transfer to an intermediate or intensive care unit may be indicated. Interventions such as embolization may be required. Moreover, a therapeutic endoscopy can be performed when intraluminal bleeding is present. Severe cases might also warrant a reoperation. Grade C PPH that comprises patients with delayed severe PPH is the most serious type and is potentially life threatening. The cause is usually a pseudoaneurysm and the bleeding occurs after discharge from hospital. Patients are clinically unstable due to massive hemorrhage leading to hypovolemia. Fluid resuscitation and blood transfusions are immediately required to stabilize the patient. The patient is transferred to an intensive care unit, and efforts are targeted toward finding and treating the source of bleeding [77]. Emergency angiography can be performed to locate the site of bleeding, and embolization can be carried out if pseudoaneurysm or confirmed contrast leak is present [86]. In case all interventional modalities prove futile, re-laparotomy is indicated to identify and control the source of bleeding.

24.6 Other Complications

In addition to the aforementioned complications, PD is also associated with biliary complications, chyle leakage, cardiac events, and pulmonary complications. Chyle leak is a rare complication involving the pathological leakage of lymphatic fluid into the abdominal cavity. This fluid is rich in triglycerides, nutrients, lymphocytes, and immunoglobulins [89]. Therefore its leakage and the subsequent chylous ascites lead to nutritional depletion, dehydration, electrolyte imbalance, and weakening of the immune system. Chyle leakage after pancreatic surgery is usually seen after extensive retroperitoneal dissection of lymph nodes [90]. This is because the cisterna chyli is located anterior to the first and second vertebrae at the same level of the pancreas; therefore, there is a high chance of damage during extended retroperitoneal lymph node dissection

[91]. Moreover, manipulation of the para-aortic area, retroperitoneal invasion of tumor, and manipulation of the root of superior mesenteric artery have also been reported to be risk factors for chyle leakage [89, 92]. The treatment for chyle leakage consists of using low-fat diet or TPN. Somatostatin analogues can be used if the leak is not controlled by dietary intervention. The use of external beam radiotherapy has been reported in literature with varying results for cases refractory to dietary interventions and the use of somatostatin analogue [93]. Bile leakage is defined as an increase in bilirubin concentration in the drain fluid of at least three times higher than serum bilirubin on or after POD3 or if radiologic or operative interventions are needed due to collection of biliary fluid or bile peritonitis [94]. The cause is usually related to surgical technique. Cholangitis is another complication that can develop both in the acute and delayed setting. A contaminated surgical field may give rise to acute cholangitis where as a stricture of the hepaticojejunostomy might cause delayed cholangitis. Cultures from the blood and bile are used to direct antibiotic therapy in both cases [95, 96]. Other complications after PD include cardiac events and infectious complications such as pneumonia [1].

Conclusions

Pancreaticoduodenectomy is a complex surgical procedure and remains only a curative management for patients with resectable pancreatic cancer. Although over the last few decades modifications in surgical technique and perioperative care have resulted in a significant reduction in the associated mortality, the morbidity associated with PD still remains high. Recognition of high-risk patients, early diagnosis, and accurate management based on available protocols is crucial in reducing the impact of these complications on the quality of life and outcomes of these patients as well as the related healthcare costs. Further research on improvements in surgical techniques and perioperative care are still required.

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25 Postoperative Management in Patients Undergoing Major Pancreatic Resections

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25.1 Introduction

Pancreatic surgery has been traditionally considered a high-risk surgery. Centralization of pancreatic resections in "high-volume centers" has contributed to the drastic reduction of perioperative fatal complications [1]. In these institutions patients undergoing pancreatic surgery are managed by a multidisciplinary team that includes specialized surgeons, anesthetists, radiologists, gastroenterologist, physiatrists, and nurses. Standardized protocols for the perioperative management of these patients have been developed on the basis of evidence-based principles with significant improvements on the final surgical outcomes [2, 3].

25.2 Fluid and Electrolyte Management

Principles of fluid administration in a patient undergoing major abdominal surgery are challenging. While an insufficient fluid resuscitation may lead to organ hypoperfusion [4], a positive fluid balance impacts negatively on general postoperative conditions as well as on the intestinal motility and the anastomotic healing [5]. An increased amount of fluid administration causes interstitial fluid overload leading to pulmonary complications and bowel wall and parenchymal edema, increasing the risk of postoperative ileus, delayed gastric emptying, and anastomotic dehiscence. For these reasons, several studies conducted on the liver, colorectal and pancreatic surgery support a postoperative restrictive fluid management (near-zero fluid balance) [5, 6]. Use of epidural analgesia can complicate the maintenance of a near-zero fluid balance by determining vasodilatation and hypotension that could be interpreted as fluid depletion. In order to avoid an unnecessary fluid overload, vasopressor should be considered for the management of epidural-induced hypotension [3]. Although colloids produce a better volume expansion and less interstitial space overload than crystalloids, there is no evidence that colloid infusion results in a better clinical outcome [7]. Crystalloids are indeed usually preferred in the routine clinical practice, avoiding the well-known risk of acute kidney injury during colloid infusion [7]. Regarding the type of crystalloids, a recent study shows that balanced infusions should be preferred than an excessive use of 0.9% saline that is associated with an overall increase of postoperative complications [8]. A possible postoperative

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fluid protocol consists of continuous fluid infusion with balanced salt solution at 1–2 mL/kg/h. In case of postoperative hypotension not hypovolemia-related, it is recommended to not exceed with fluid infusion, preferring the use of etilefrine (bolus 1 mg, up to 10 mg) or dopamine (5 mcg/kg/min) when not contraindicated [3].

25.3 Feeding

Although the oral intake promotes the pancreatic juice secretion, the Enhanced Recovery After Surgery (ERAS) Society and ASPEN guidelines suggest that its is feasible and safe also after pancreatic surgery [3, 9]. When compared to other feeding routes such as total enteral nutrition (TEN) and total parenteral nutrition (TPN), the early oral intake has been was found be associated with a shorter length of hospital stay and time to resumption to a normal diet. Also, TEN and TPN are associated with several complications. The nasojejunal tube dislodges within the first week after surgery in ~36% of patients, the jejunostomy might cause bowel torsion, whereas TPN has an increased risk of infection [10–13]. The early oral feeding, with a stepwise diet starting from a clear liquid diet to a diet without restriction, is therefore recommended. However, if the early oral intake is not tolerated or additional nutritional support is required, TEN is preferred to TPN. Several studies have shown that TEN prevents the atrophy of the gastrointestinal mucosa preserving the intestinal bacterial flora architecture and reducing the bacterial translocation [17, 18]. Also TEN has a reduced risk of infection and metabolic disorder compared to TPN [13–16].

25.4 Antimicrobial Prophylaxis

Antimicrobial prophylaxis during surgical procedures aims to reduce the incidence of surgical site infections (SSI). In this setting antibiotic should be administered in a single dose as near as possible the incision of the skin, and an extra dose should be administered after 3–4 h from the beginning of the operation according to the antibiotic half-life [19, 20]. The Surgical Care Improvement Project (SCIP) workgroup in 2006 developed guidelines for antimicrobial prophylaxis to reduce wound infections and suggested for abdominal surgery the use of cefotetan, cefazolin, cefoxitin, or ampicillin-sulbactam [21]. The perioperative antibiotic choice as recommended is however not specific for pancreatic surgery. Complex procedures as PD include surgical reconstruction with multiple anastomoses, and they can be characterized by intraoperative biliary and/or enteric contamination.

Also, the preoperative presence of biliary stent for jaundice palliation is per se associated with an increased rate of SSI that in this population reach the 26–46% [23, 24]. Obstructive jaundice leads to biliary stasis and the bacterial proliferation, while the endoscopic procedures cause the ascending microbial contamination from the duodenum. During PD, the section of the bile duct and the bile spillage cause the contamination of the peritoneal cavity. For this reason, the patient with a biliary stent should undergo a broader empiric antimicrobial prophylaxis for a more extended period after surgery [25–27]. Finally, the intraoperative bile sampling can also help to identify targeted antimicrobial therapy in case of SSI [27].

25.5 Thromboprophylaxis

Cancer patients undergoing major abdominal surgery have a doubled risk of postoperative deep vein thrombosis and more a tripled risk of fatal pulmonary embolism compared to nonneoplastic patients [28]. Postoperative changes in the coagulatory/fibrinolytic balance in favor of coagulation persist beyond the first 7–10 days following surgery with a 25% risk of venous thromboembolism at 4–6 weeks [29]. According to the European Society for Medical Oncology (ESMO) [30] and ERAS [3] guidelines, extended thromboprophylaxis with low molecular weight heparin (LMWH) is recommended for all patients undergoing pancreatic surgery. Because of the concerns on postoperative bleeding, the ACCP

guidelines [31] suggest instead to stratify LMWH therapy according to the bleeding risk. In patients at high risk for major bleeding, is suggested the use of mechanical prophylaxis only, whereas the pharmacologic one should be postponed until the risk of bleeding decreases.

25.6 Somatostatin and Its Analogues

TPostoperative pancreatic fistula (POPF) is the primary cause of morbidity and mortality following pancreatic surgery, and several strategies have been employed to reduce its incidence. The active exocrine secretion of pancreatic enzymes plays a crucial role in the POPF development. Somatostatin is a 14-amino acid peptide that inhibits pancreatic exocrine, biliary, and small bowel secretions and increases water absorption [32]. When POPF occurs, somatostatin works by reducing its output with potentially positive effects on its natural course. Because somatostatin has a short half-life (1–2 min), synthetic analogues such as octreotide and pasireotide have been developed (with a half-life of 120 min and 11 h, respectively) [32, 33]. Somatostatin analogues allow intermittent subcutaneous dosing schedules and differ from each other in the binding profile for somatostatin receptors [32, 33]. Several randomized controlled trials have been conducted to demonstrate the benefit of somatostatin and its analogues in reducing POPF incidence and severity. However, the results from these studies were conflicting and difficult to compare because of the heterogeneity in outcome definition, drug and schedule employed, and in surgical procedures [34, 35]. Finally, a Cochrane systematic review [35] comparing the use of somatostatin analogues with a non-somatostatin group reported a lower overall postoperative complications in the interventional group, although no differences were observed in POPF rate.

Recently, a randomized placebo-controlled trial on pasireotide demonstrated a significant reduction of clinically relevant POPFs in the interventional group (7.9% vs. 16.9%) with no grade C fistula occurring [33]. However, further randomized trials are advocated before to recommend Pasireotide as standard prophylaxis in patients undergoing pancreatic surgery.

25.7 Mobilization

Prolonged bed rest after surgery is considered as a risk factor for several postoperative complications. Early mobilization (EM) protocols are widely accepted in order to reduce the risk of thromboembolism, pneumonia, muscle wasting, and physical deconditioning [3]. In addition, EM positively impacts on the early return of the bowel function and on reducing the hospital length of stay. A practical approach consists of instructing patients on the benefits of early mobilization using written protocols with specific day-to-day postoperative specific targets.

According to our institutional protocols for postoperative care after pancreatic surgery, patients assume the sitting position 6 h after surgery and start bed gymnastic and ambulation on POD 1. Facilitation of mobilization is provided by a nurse or nursing assistant (Fig. 25.1). On POD 2 the duration of mobilization and ambulation is increased. On POD 3 patients spend most of the day outside the bed achieving a complete mobilization. Patients with specific difficulties in the physical functioning are referred to a physiotherapist, while no evidences suggest that allocating specific staff for patients with normal functioning provides additional benefits over usual EM protocols [36]. Analgesia should be balanced to provide adequate pain relief to allow EM.

25.8 Drain Management

Because of the high incidence of pancreatic fistula, one or more abdominal drainages are usually placed intraoperatively in the proximity of the pancreatic anastomosis or stump. However, some studied showed that the drain placement following pancreatic surgery is associated with an increased risk of infection due to the presence of external communication. Some authors also

report that the drain might extert a mechanical pressure on the pancreatic anastomosis provoking iatrogenic damage and the pancreatic leakage [37, 38]. The routinely lack of abdominal drainage following PD is associated with an increased postoperative rate of complications and mortality and therefore is not recommended [39]. However, drain management should be tailored to the patients risk of developing POPF. In patients with a negligible/low risk according to the Fistula Risk Score (Table 25.1), drainless PD has been demonstrated to be safe and feasible [41, 42].

Patients characterized by a moderate/high risk must be routinely drained. In these, the timing of drain removal should be driven by patient's clinical condition and by the presence of a fluid rich in amylase, indicating the presence of a POPF (Fig. 25.1) [43– 45]. According to our validated protocol [38, 42], patients with a POD 1 drain fluid containing less than 5000 UI/L are candidate to the early drain removal on POD 3. Patients with drain in place after POD 3, should be tested again for the amylase content on POD 5, and those with <200 UI/L should be considered for drain removal. Protocol deviations are possible in case of drain sinister appearance (dark brown to greenish bilious fluid, to milky water to clear "spring water" that looks like pancreatic juice) or development of clinical warning signs indicative of other potential complications. The application of this protocol in our institution has resulted in a significant reduction of morbidity, readmission rate, hospital stay, and costs [38]. However,

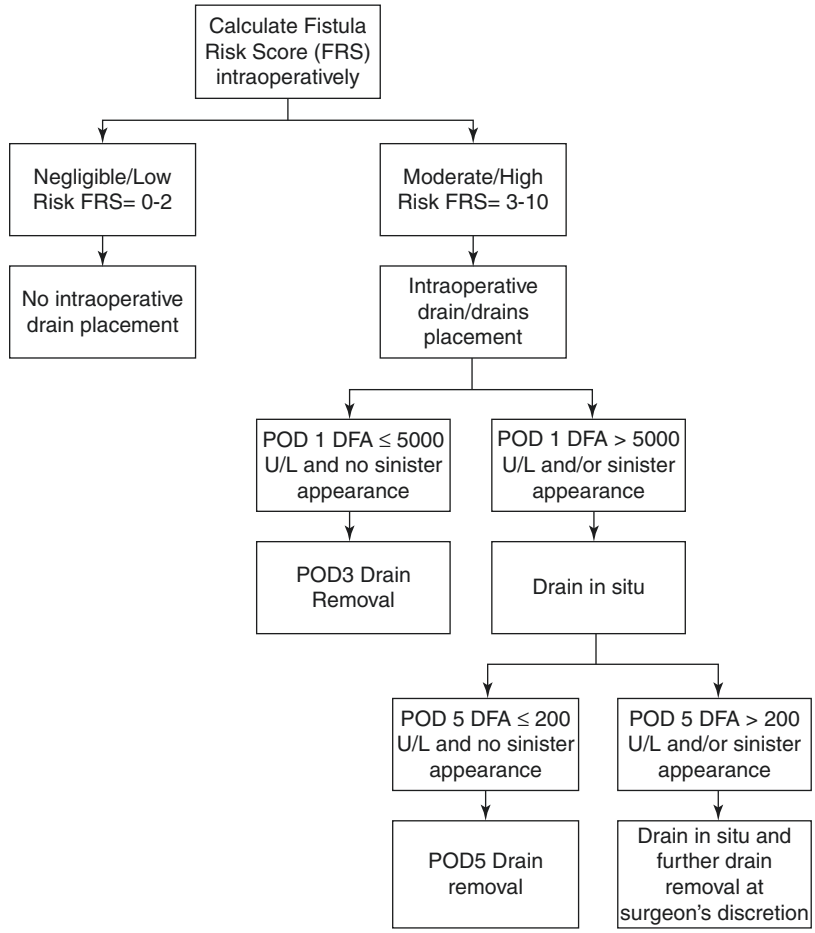

Fig. 25.1 Proposed drain management protocol: selective drainage for patients with moderate/high risk to develop pancreatic fistula and its early removal according to POD 1 drain fluid amylase (DFA) and clinical condition [41, 42, 52]

variability in amylase test exists among laboratories, therefore the amylase cutoff should be calibrated accordingly.

25.9 Radiology

Routine radiological assessment after pancreatic surgery is not recommended [46, 47]. Surgical complications including pancreatic fistula can be suspected on the basis of the clinical and laboratory findings, and cross-sectional imaging should be reserved when a deviation from the normal postoperative course occurs [47]. Routine postoperative contrast-enhanced CT after PD has a lower sensitivity and specificity for pancreatic fistula compared to drain fluid amulase measurement [43, 47, 48], while routine postoperative US detects abdominal collections that are asymptomatic and with an uncertain clinical meaning in about 21% of patients [49]. These collections are arranged around the pancreatic anastomosis or in the surgical bed, and in the majority of cases, no further interventions are necessary. Only 35% of the cases require an interventional procedure to drain collections when other worrisome clinical features as fever and leukocytosis are developed [49, 50].

A fistulography should be performed to evaluate the eventuality of the drain decubitus on the pancreatic anastomosis in patients maintaining drains for a long-time showing an unexpected "sinister" effluent despite an earlier amylase negative drain fluid. This procedure consists in the injection of the contrast agent through the drain while dynamic fluoroscopy is performed. If there is a decubitus of the drain, the fistulous tract connecting the drain to the intestinal lumen is visualized. In this case a 3–5 cm drain retraction permits to separate the drain from the anastomosis promoting its healing [51].

Table 25.1 FRS for the prediction of CR-POPF after pancreatoduodenectomy

Risk factor	Parameter	Points
Gland texture	Firm	0
	Soft	2
Pathology	Pancreatic adenocarcinoma or pancreatitis	0
	Ampullary, duodenal, cystic, islet cell, etc.	1
Pancreatic duct diameter	≥5 mm	0
	4 mm	1
	3 mm	2
	2 mm	3
	≤1 mm	4
Intraoperative blood loss	≤400 ml	0
	401–700 ml	1
	701–1000 ml	2
	>1000 ml	3
		Total 0–10 points

Reproduced from Callery et al. [40]

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26 Pathology Reporting of Resected Pancreatic/Periampullary Cancer Specimen

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Abbreviations

AJCC	American Joint Committee on Cancer
BDM	Bile duct margin
CAP	College of American Pathologists
CDP	Cephalic duodenopancreatectomy
CRM	Circumferential resection margin
DBDC	Distal bile duct carcinoma
DP	Distal pancreatectomy
IPMN	Intraductal papillary mucinous neoplasm
ISGPS	International Study Group of Pancreatic Surgery
ITPN	Intraductal tubulopapillary neoplasm
JPS	Japan Pancreas Society
LN	Lymph node
LNR	Lymph node ratio
PanIN	Pancreatic intraepithelial neoplasia
PDAC	Pancreatic ductal adenocarcinoma
PNM	Pancreatic neck margin
PUPM	Posterior surface of the uncinate process margin
PV-SMVM	Portal vein-superior mesenteric vein margin
RCPA	Royal College of Pathologists of Australasia
RCPUK	Royal College of Pathologists of the United Kingdom
SMA	Superior mesenteric artery
SMAM	Superior mesenteric artery margin
SMV	Superior mesenteric vein
SMVM	Superior mesenteric vein margin
TP	Total pancreatectomy
WHO	World Health Organization

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26.1 Introduction

Pancreatic cancer is the fourth leading cause of cancer-related death in developed countries with an overall 5-year survival rate of 7% [1] and is expected to be the second cancer cause of death by 2020 [2]. Surgery still remains the best therapy for potentially curative purposes, but only 15–20% of the patients are candidates for resection [3]. Even if patients undergo surgical resection, recurrences are common, and cure,

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despite advances in medical therapy, is infrequent [4, 5].

In pancreatic and periampullary neoplasms, some important prognostic factors are derived from pathological examination of the surgical specimen, such as tumor size and location, site of origin, degree of differentiation, lymphovascular and neural invasion, lymph node involvement, and surgical margin status [4–16]. However, the real relevance of surgical margins as a prognostic factor in pancreatic cancer is uncertain due to the great variability of positive margin rates in the literature (from 10% to 76–85%) [12, 17, 18]. One of the main turning points on this issue was the publication of a study by Verbeke et al. [17] in which it was highlighted that the R1 rates (rate of microscopic involved margins) increased significantly (from 53% to 85%) after two main facts: the use of a standardized protocol based on axial slicing and the definition of R1 as tumor invasion within 1 mm from the margin. Subsequently many other authors [18–26] have also shown this increase in R1 rates after applying a conscientious pathological sampling.

Despite the fact that the first voices advocating for a standardized protocol for pancreatic cancer specimens date from 1996 [27], the lack of consensus in some relevant aspects of terminology and methodology is still a reality which makes it difficult to understand the real prognostic significance of margin involvement and continues to be the main obstacle for homogenized study results which could provide robust data for patients care. However, many efforts are being made in this regard, and according to Verbeke [28] and paraphrasing his own words, "we are entering in a new era in which meticulous and standardized pathology examination is a recognized prerequisite for obtaining robust and reproducible data. It highlights the responsibility, first and foremost of the profession of pathology, to ensure that high-quality pathology examination of pancreatic resection specimens becomes established practice."

Pancreatic ductal adenocarcinoma (PDAC) is the most common type of pancreatic cancer, and the literature frequently addresses pancreatic cancer as synonym of PDAC because of its frequency. Periampullary cancers (ampullary, distal bile duct carcinomas (DBDC) and duodenal cancers within the region of the papilla) develop in the same anatomical area (pancreatic head) and are sometimes included in pancreatic studies [29]. They are removed by the same surgical procedure and for that reason need to be considered in the pathological handling of pancreatic specimens, with only a few further details. The same considerations can be applied to other histological subtypes such as intraductal papillary mucinous neoplasms (IPMN), intraductal tubulopapillary neoplasm (ITPN), and other cystic pancreatic tumors.

26.2 Main Controversies in Handling and Reporting Periampullary and Pancreatic Head Cancer Specimens

One of the main problems in handling pancreatic specimens is the complexity of the anatomy of the pancreatic area, which requires familiarity. However, the inconsistent descriptions and diverse terminology together with the lack of detailed consensus guidelines make pathologic evaluation difficult. A recently increasing interest in margin status of pancreatic cancer specimens regarding basic concepts that still remains unsolved is being seen not only from the pathologist's point of view but also for the clinical implications in providing patients with the best possible care.

26.2.1 Margin or Surface: That Is the Question

In a recent publication by the International Study Group of Pancreatic Surgery (ISGPS) [3], pathological protocol and reporting method was one of the five main issues addressed. The consensus statement was that seven margins should be reported and designated as anterior, posterior, medial, or superior mesenteric vein (SMV) groove, superior mesenteric artery (SMA), pancreatic transection, bile duct, and enteric.

The importance of pancreatic margins is also clearly evidenced by pathologists' great number of attempts to standardize its mapping and description [17, 18, 21, 24, 26, 30–36]. However, the terminology, as well as margins routinely analyzed and reported, varies greatly in the literature [31, 34, 36, 37] (Table 26.1). These differences in terminology could be partially explained by the authors' preferences. Some of them prefer an anatomical-based approach using terms like "uncinate margin" and "vascular groove/bed," whereas others prefer to focus on the adjacent vascular structures giving names such as "superior mesenteric artery margin" (SMAM) or "superior mesenteric vein margin" (SMVM) [17, 18, 21, 24, 26, 30–34, 36, 38–41]. Indeed, some institutions only recommend inking and cutting sections in relation to the margin closest to the tumor [40, 41], while others prefer to routinely analyze the full circumferential resection margin (CRM) [18, 19, 38, 39]. Some studies on this topic [37, 42, 43] reveal the disagreement among institutions and guidelines' lack of adherence, which, not surprisingly, is why some pathologists do not adhere to the pathologist protocol reports.

Perhaps the initial question in an attempt to explain these discrepancies should be how to define a surgical margin. This point is very well described by Ethun and Kooby [37] who differentiate three ways of surgical manipulation techniques during pancreatic surgery: transection, dissection, and mobilization. A transection margin is clearly understood and almost universally accepted for pancreatic neck margin (PNM), bile duct margin (BDM), and luminal or intestinal margins [36, 37]. However, according to these authors,

Table 26.1 The wide variety of terms used in the published literature

Margins or surfaces (terms more commonly accepted)	Definition	Synonyms
Luminal margins (proximal gastric or duodenal and distal jejunal)	Gastrointestinal segment where the surgeon transects	–
Bile duct margin (BDM)	Common bile duct or common hepatic duct margin	–
Pancreatic neck margin (PNM)	Pancreatic tissue sectioned by the surgeon. The pancreatic duct can be identified in the middle. It is limited by the SMVM at its left edge	– Pancreatic duct margin – Distal resection margin – Pancreatic transection margin
Superior mesenteric vein margin (SMVM)	Concave-shaped with a smooth, glistening surface where the portal vein and the mesenteric vein are laid, placed between the SMAM and PNM. It is often flanked by clips on small veins that drain from the pancreatic head into the SMV	– Vascular bed – Vascular groove – Part of medial CRM
Superior mesenteric artery margin (SMAM)	Relatively irregular small area of soft tissue that faces the SMA delimited by SMVM at its left edge. On the right side joined to the posterior surface in an acute angle	– Uncinated margin – Retroperitoneal margin – Interior-posterior margin – Part of medial CRM
Posterior margin/surface	Smooth and slightly fibrous surface delimited by duodenum and SMAM, which overlies the aortocaval groove	– Posterior CRM – Part of uncinated margin – Part of posterior CRM – Deep retroperitoneal posterior surface – Inferior vena cava margin
Anterior surface	Adipose tissue covered by serosa delimited by the duodenum, PNM, and SMVM	– CMR: anterior

BDM bile duct margin, *CRM* circumferential resection margin, *PNM* pancreatic neck margin, *SMA* superior mesenteric artery, *SMAM* superior mesenteric artery margin, *SMV* superior mesenteric vein, *SMVM* superior mesenteric vein margin

the difference between dissected and mobilized margin is less clear, especially when surfaces that can usually be separated by peeling off along their embryologic planes in an unspoiled state are disrupted by fibrosis, inflammation, or tumor invasion. In these conditions, mobilized tissues could be interpreted as margins or surfaces and consequently handled and reported [37]. Table 26.2 details the differences in margin approach in the published literature over the last years.

26.2.1.1 Anterior Surface

The anterior aspect (Fig. 26.1a) is differently interpreted by the main pancreatic experts. Its consideration as a dissection margin in the definition of "radicality" was defended by the Japan Pancreas Society (JPS) [56, 57]. Its involvement has been associated with tumor recurrence and decrease of overall survival [58, 59]. Although the assessment of anterior margin has also been introduced in Europe and in some groups of North America [17, 18, 38, 60], it is considered mostly as a surface. It is less frequently involved (10–15%) and more rarely in isolation [17–19, 22]. For all of these reasons, some authors establish a 0 mm clearance to consider involvement [18, 19, 38, 39]; others prefer not to consider it as R1 resection if only the anterior surface is involved [21], and yet other authors do not include it in margin assessment [15, 26, 40, 41, 51]. Even if consensus is not achieved regarding the definition (margin or surface) and the involvement rate is low, it should be documented due to the risk of recurrence [18, 19, 36, 38, 39].

26.2.1.2 Posterior Margin/Surface

The posterior margin (Fig. 26.1b) is defined by the Royal College of Pathologists of the United Kingdom (RCPUK) protocol [38] as the fibrous but smooth surface of the pancreatic head overlying the aortocaval groove. The protocol of the Royal College of Pathologists of Australasia (RCPA) [39] describes this margin/surface as a smooth non-peritonealized posterior surface of the uncinate process, not including the SMAM. This posterior-right face of the uncinate aspect is mostly considered as margin (Table 26.2). However, some authors [36, 40] prefer to consider it as surface due to the fact that it is covered by serosa in a very similar manner to the anterior surface, even if it should be submitted and reported.

26.2.1.3 Medial Margin

The medial or vascular margin (Fig. 26.2) refers to the area that faces the superior mesenteric vessels. It can be subdivided in two areas or margins. The first area is characterized by a shallow and slightly glistening concavity usually delimited by clips [19]. This part of the margin faces the SMV, and for that reason, it is now widely called SMVM [38, 39]. Sometimes, a segment of vein can be included in the pancreatic specimen. The second area is the posterior peripancreatic adipose tissue that faces the SMA. This margin has been given many terms such as retroperitoneal, uncinate, or posterior margin, often equivocal and confusing [37, 61] (Tables 26.1 and 26.2).

The site of margin involvement is clearly influenced by the tumor origin and size [22, 29]. Medial (SMVM and SMAM) and posterior margins are the most important since they are the most frequently affected in PDAC [18, 19, 21, 26, 30, 31]. The involvement of anterior surface is less common, and despite the fact that the presence of tumor cells on this surface is likely to increase the risk of local tumor recurrence [18, 59], its impact in outcome seems not to be very relevant [24, 26]. These observations are also applicable to distal bile duct carcinoma (DBDC) [22]. However, margin involvement in ampullary carcinomas is less frequently observed [10, 11, 14, 16, 17, 22, 30, 62]; this fact could be explained by its greater distance to margins and its heterogeneity in size distribution in the studied series (smaller size rate in ampullary carcinomas compared to PDAC or DBDC). When dealing with an intraductal tumor (IPMNs or ITPNs) or a DBDC, the PNM and BDM could be more crucial [40], but they usually are studied previously during intraoperative assessment. In DCBD carcinomas arising in the medial segment of the bile duct, which is partially extrapancreatic and surrounded by soft tissue (so-called radial periductal margin), are important to evaluate this latter tissue but are usually not analyzed routinely in pancreatic specimens [61, 63].

Table 26.2 Different approaches to margin reporting in the literature over the last years

	Margins/surfaces			
Study	Anterior	SMVM	SMAM	Posterior
Staley et al. [27]	–	–	Retroperitoneal margin	–
Lüttges et al. [44]	–	–	Retroperitoneal resection margin	–
Verbeke et al. [17] Verbeke et al. [19] Menon et al. [22]	Anterior CRM	SMV groove or medial CRM	Posterior CRM	
Howard et al. [45]	–	–	Retroperitoneal soft tissue margin	
Raut et al. [46]	–	–	SMAM (retroperitoneal margin)	–
Esposito et al. [18]	Anterior surface	Medial margin	Posterior margin	
Westgaard et al. [30]	–	–	Retroperitoneal resection margin	
Campbell et al. [21]	Anterior surface (not margin)	Medial or SMVM	Posterior margin	
Khalifa et al. [31]	–[a]	The groove (vascular bed) surface	Uncinate margin	Uncinate process surface
Chang et al. [15]	Anterior surface (not margin)	PV/SMVM	SMAM/retroperitoneal margin	–
Gaedcke et al. [32]	Anterior (ventral) surface	SMV groove	Mesopancreas	Posterior (dorsal) surface
Jamieson et al. [24] Jamieson et al. [47]	Anterior surface	Medial transection margin (including SMV groove)		Posterior surface
Gnerlich et al. [48]	–	PV groove	Uncinated margin	Posterior margin
Rau et al. [33]	Anterior surface	Medial margin (transected superior mesenteric plexus and SMV groove)		Posterior margin
John et al. [49]	Anterior surface	PV/SMVM	Posterior margin	
Kimbrough et al. [50]	–	–	SMA/uncinate margin	
Konstantinidis et al. [51]	Anterior surface (not margin)	–	Uncinate/SMAM	Retroperitoneal/posterior margin
Sugiura et al. [52]	–	–	SMAM	Posterior margin
Maksymov et al. [34]	–[a]	SMVM	SMAM	PUPM
Delpero et al. [26]	Anterior surface (not margin)	PV-SMVM	SMAM	Posterior margin
		Medial vascular margin: PV-SMVM + SMAM		

(continued)

Table 26.2 (continued)

Study	Margins/surfaces			
	Anterior	SMVM	SMAM	Posterior
Gómez-Mateo et al. [35]	Anterior surface (not margin)	Vascular groove	Posterior margin	–
Adsay et al. [36]	Anterior free surface	Vascular bed (surface)	Uncinate margin	Posterior free surface
Mathur et al. [53]	Anterior surface	–	SMAM	Uncinate and posterior margin
Pang et al. [54]	Anterior surface	SMV bed	Periuncinate/medial/retroperitoneal margin	True posterior margin
Gebauer et al. [55]	Anterior aspect	SMV groove/medial/uncinate		Posterior aspect
JPS [56]	Anterior surface	Retropancreatic surfaces		
RCPUK [38]; Verbeke and Menon [20]	Anterior surface	SMVM	SMAM	Posterior margin
		Medial CRM: SMVM + SMAM		
RCPA [39]	Anterior margin	SMVM/vascular groove	SMAM	Posterior margin
CAP [40]	–	Vascular groove	Uncinate (retroperitoneal/SMAM)	–
AJCC 7th [41]	–	–	SMAM	Posterior margin
ISGPS consensus [3]	Anterior margin	Medial or SMVM	SMAM	Posterior margin

AJCC American Joint Committee on Cancer, *CAP* College of American Pathologists, *CRM* circumferential resection margin, *ISGPS* International Study Group of Pancreatic Surgery, *JPS* Japan Pancreas Society, *PUPM* posterior surface of the uncinate process margin, *PV* portal vein, *PV-SMVM* portal vein-superior mesenteric vein margin, *RCPA* Royal College Pathologists of Australasia, *RCPUK* Royal College of Pathologists of the United Kingdom, *SMA* superior mesenteric artery margin, *SMAM* superior mesenteric artery margin, *SMV* superior mesenteric vein, *SMVM* superior mesenteric vein margin

[a]According to authors' opinion, the anterior margin is present in a pylorus-preserving PD and absent in a standard Whipple procedure [34]

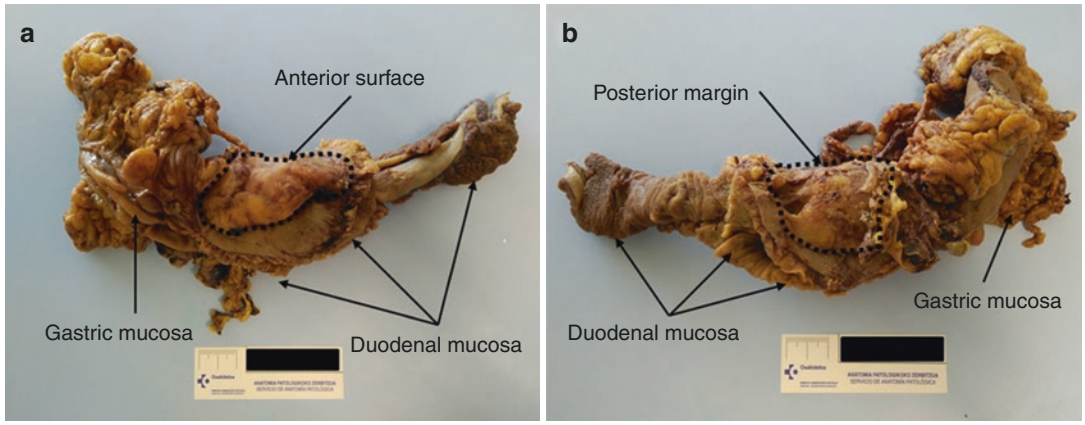

Fig. 26.1 A cephalic duodenopancreatectomy (CDP) specimen after fixation in formalin. Gastrointestinal lumen is opened. (**a**) Anterior view. Anterior surface is an adipose-rich tissue covered by a bright and smooth serosa layer (area comprised into the *discontinuous black line*). (**b**) Posterior view. Posterior margin is the smooth and slightly fibrous serosa area (comprised into the *discontinuous black line*)

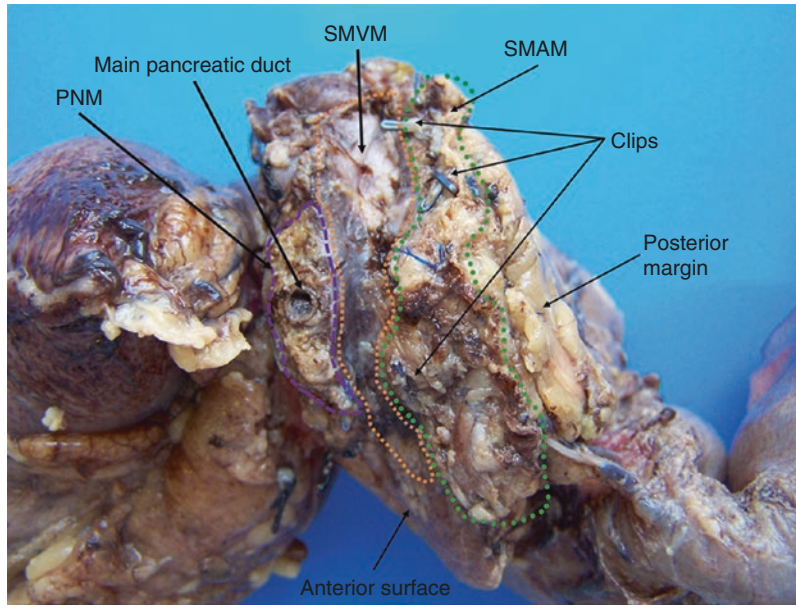

Fig. 26.2 Posterosuperior view of a CDP specimen. From this view we recognize pancreatic neck margin (PNM) (into the *discontinuous violet line*) and both vascular margins: superior mesenteric vein margin (SMVM) and superior mesenteric artery margin (SMAM) (delimited by *discontinuous orange* and *green lines*, respectively). Main pancreatic duct is seen in the middle of PNM, in this case dilated. The division line between SMVM and SMAM is often highlighted by some clips. Posterior margin is also recognized from this view

Summarizing, the recommendations of the main pathologist institutions are as follows:

- The RCPUK includes in its histopathological report the transection margins (gastric, duodenal, pancreatic, and bile duct), the dissected margins (SMV, SMA, posterior), and the anterior surface [38].
- The RCPA protocol recommends reporting the distance to the following margins/surfaces:

pancreatic transection, SMAM, posterior margin, SMVM/vascular groove, anterior margin, bile duct, proximal intestinal/gastric, distal intestinal, and other margins/surfaces [39].

– The College of American Pathologists (CAP) suggests in its template for cephalic duodenopancreatectomy (CDP) reporting PNM, uncinate (retroperitoneal/SMA) margin, BDM, proximal and distal margins, and other margins (only if applicable). Anterior and posterior surfaces are reported in the microscopic tumor extension assessment but not in margin section [40].

26.2.2 Differences Among Slicing Techniques and Tissue Sampling

The macroscopic handling of pancreatic specimens has a great impact on histologic examination. The extent of tissue sampling is directly related to the accuracy of the margin assessment [17]. In some protocols, the slicing technique is not well described, and the need to ink some of the margins and submit them is only superficially addressed [40, 41, 44]. In fact, sometimes only the tumor point closest to the margin is recommended to be submitted specifically for microscopic evaluation. However, if only a few samples are taken from the tumor in relation to the closest margin, the assessment of margin involvement could be underestimated. In pancreatic tumors, limits are quite difficult to identify macroscopically as is to distinguish them from fibrosis, chronic inflammation, or pancreatic atrophy [19]. Moreover, the growth pattern at the periphery of the tumor is highly dispersed in PDAC as compared with other tumor types [64]. For these reasons, meticulous gross inspection and extensive tissue sampling are needed.

A wide range of different dissection techniques is being used, with advantages and disadvantages, some of them based on the pathologist's preference or on tradition [19]. The main slicing techniques (with their variations) can be classified according to the main axis: bivalving, bread loaf slicing, and axial slicing (Fig. 26.3).

26.2.2.1 Bivalving and Multivalving Slicing Technique

This method has been used for many years [44, 65] and is still used in some institutions [36]. It consists in horizontally cutting the pancreatic specimen after probing both ducts (pancreatic main duct and common bile duct). Although it may seem more adequate for intraductal neoplasms, this method is not optimal for assessing the circumferential margins [19]. Generally, more dissection planes to take samples are needed, making reconfiguration of the specimen challenging.

26.2.2.2 Bread Loaf Slicing Technique

This method [60] is based on serial slicing perpendicular to the pancreatic major axis that results in incomplete and fragmented sections of the pancreas, making it difficult to evaluate the ampullary area. Instead of parallel slicing, the JPS [56] suggested serial slicing perpendicular to an axis that follows the curvature of the pancreatic head, also problematic in terms of changing cut planes and producing irregular sections [19].

26.2.2.3 Axial slicing technique

This technique uses a slicing plane perpendicular to the longitudinal axis of the second portion of the duodenum. This approach has been introduced and developed mainly in Europe [17, 18, 21, 22, 24]. The main advantage is its simplicity: it is easy to perform and to learn through training. It is useful independently of tumor location or origin. Indeed, this technique produces a great number of sections, thus allowing macroscopic inspection of the main structures (ampulla, pancreatic main duct, common bile duct, etc.) and the full margin surface. It is possible to obtain perpendicular sections for all relevant margins for assessing the distance to the tumor, and it is easy to identify and classify regional lymph nodes [61].

Although no method has proved to be superior, some of them are not as optimal as desired for pathology reporting, especially for margin assessing, and are partially responsible of variability in literature results [17, 18, 37].

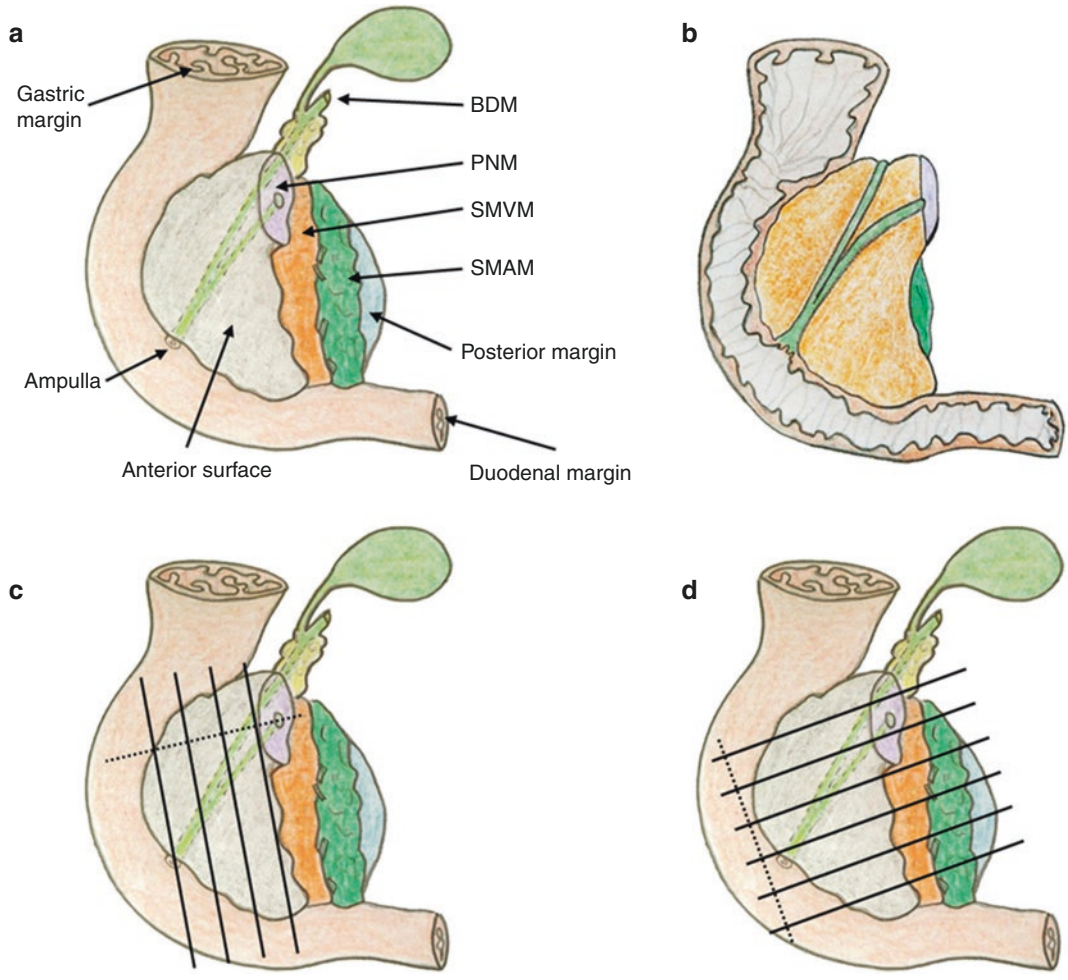

Fig. 26.3 Schematic design of a CDP specimen (Modified from Verbeke et al. [19]). (**a**) Complete specimen where all margins are represented by a color code—anterior surface in *gray*, PNM in *violet*, SMVM in *orange*, SMAM in *green*, and posterior margin in *blue*. Gastric, duodenal, and BDM are also signaled. (**b**) CDP specimen after bivalving slicing technique. Both ducts are probed and horizontally sliced. (**c**) Bread loaf slicing technique is represented. Serial sections (*black lines*) are made perpendicular to the pancreatic major axis (*discontinuous line*). (**d**) Axial slicing technique. The slicing lines (*black lines*) are perpendicular to the longitudinal axis of the second portion of the duodenum (*discontinuous line*)

26.2.3 Margin Involvement Is Not Only a Quality of Surgery

Microscopic involvement of resection margin (R1) is considered a poor prognosis indicator in solid tumors [26]. R1 resection has been reported to be an independent predictor factor of poor outcome in PDAC in several studies [4, 5, 8, 12, 13, 22, 24, 30, 33, 45, 48, 66–70]. However, results in other studies do not confirm this relevance [11, 46, 71].

R status is commonly regarded as a quality indicator of a surgical procedure, but in PDCA it is complex and multifactorial [37]. As seen before, reported margin positivity rates range widely (10% to 85%) [12, 17, 18]. These contradictory results are, in large part, due to the disagreement in the pathological assessment. The gross handling and slicing technique used, the number of samples taken, and the minimum clearance in mm used to define margin involvement enormously influence the rate of R1 [19, 21, 26, 61] (Table 26.3).

Table 26.3 Comparison of R1 rates and other related parameters in patients with resected pancreatic ductal adenocarcinoma

Study reference	Year	Number of patients with PDAC	R1%	R1 definition	Slicing technique	Number of margins examined
Willet et al. [72]	1993	72 (5TP)	51%	0 mm	NS	5[a]
Allema et al. [6]	1995	67	63%	0 mm	NS	NS
Yeo et al. [73]	1997	174 (11TP)	29%	0 mm	NS	5
Yeo et al. [7]	1998	149	31%	0 mm	Bivalving	5
Millikan et al. [74]	1999	84 (15TP)	29%	0 mm	NS	NS
Benassai et al. [75]	2000	75	20%[b]	0 mm	NS	5
Sohn et al. [8]	2000	616 (52DP, 38TP)	30%	0 mm	NS	NS
Van Geenen et al. [10]	2001	108	43%	0 mm	NS	NS
Neoptolemos et al. [66]	2001	541 (12% TP or DP)	19%	0 mm	NS	NS
Jarufe et al. [9]	2004	133	49.2%	0 mm	NS	NS
Schmidt et al. [11]	2004	202	20%	0 mm	NS	4/6[a]
Wagner et al. [12]	2004	211 (29DP, 17TP)	10%	0 mm	NS	NS
Howard et al. [45]	2006	226 (13DP, 9TP)	28%	0 mm	NS	4
Verbeke et al. [17]	2006	26	84.6%	≤1 mm	Axial	7[a]
Winter et al. [13]	2006	1175 (79TP, 7PP)	42%	0 mm	NS	5
Raut et al. [46]	2007	360	16.7%	0 mm	Perpendicular sections of SMAM; PNM and CBDM En face sections	3
Van Roest et al. [12]	2008	51	32%	0 mm	NS	NS
Esposito et al. [18]	2008	111	76%	≤1 mm	Axial	7
Westgaard et al. [30]	2008	40	45%	≤1 mm	Bivalving	5[a]
Campbell et al. [21]	2009	163	43.6% (0 mm) 79% (≤1 mm)	–	Axial	6[a]
Chang et al. [15]	2009	365 (70 DP)	36% (0 mm) 45% (≤0,5 mm) 51% (≤1 mm) 54% (≤ 1,5 mm) 57% (≤2 mm)	–	NS	6
Menon et al. [22]	2009	27	82%	≤1 mm	Axial	7[a]
Hatzaras et al. [16]	2010	249	18%	0 mm	NS	NS
Gaedcke et al. [32]	2010	46	63%[b] (0 mm) 82.6%[b] (≤ 1 mm)	–	Perpendicular to mesopancreatic margin (axial)	7
Hsu et al. [76]	2010	1092 (64TP)	33.2%	≤ 1 mm	NS	5
Jamieson et al. [24]	2010	148	55% (0 mm) 73.6% (≤1 mm)	–	Axial	7[a]
Liszka et al. [23]	2010	13	53.8% (0 mm) 61.5% (≤ 1 mm)	–	Axial	7
Gnerlich et al. [47]	2012	285	34%	≤1 mm	NS	5
Rau et al. [33]	2012	94	51%	0 mm	Axial	7[a]

Table 26.3 (continued)

Study reference	Year	Number of patients with PDAC	R1%	R1 definition	Slicing technique	Number of margins examined
Maksymov et al. [34]	2012	25 (1TP)	56% (0 mm) 80% (≤1 mm)	–	Longitudinally along the long axis of the CBD	7[a]
Jamieson et al. [48]	2013	217	51.2% (0 mm) 59% (≤0.5 mm) 72.4% (≤1 mm) 82.5% (≤1.5 mm) 86.2% (≤2 mm)	–	Axial	7[a]
John et al. [49]	2013	70	74,3%	≤1 mm	Axial	7
Kimbrough et al. [50]	2013	283 (30DP, 5SP)	26.8%	0 mm	En face section of each margin	3
Konstantinidis et al. [51]	2013	554 (86DP, 8TP)	28% (0 mm) 58.8% (≤1 mm)	–	Perpendicular slicing (Staley's protocol [27])	4
Sugiura et al. [52]	2013	208 (42DP, 2TP)	16% (0 mm) 19% (≤1 mm)	–	Radial 5 mm sections (Japan's method [56])	4
Delpero et al. [26]	2014	150	23% (0 mm) 61% (≤1 mm) 63% (≤1.5 mm) 71% (≤2 mm)	–	Axial	7[a]
Mathur et al. [53]	2014	448	25%	0 mm	Perpendicular sections to margins, en face for CBDM and SMAM	8[a]
Pang et al. [54]	2014	116	58%	≤1 mm	Bivalved. 1 section minimum per margin. Periuncinate retroperitoneal margin almost totally embedded	7[a]
Sabater et al. [25]	2014	68 (13DP, 8TP)	53%	≤1 mm	Axial	5
Gebauer et al. [55]	2015	118	52%	≤1 mm	Axial	6

CBD common bile duct, *CBDM* common bile duct margin, *CDP* cephalic duodenopancreatectomy, *DP* distal pancreatectomy, *NS* nonspecified, *PDAC* pancreatic ductal adenocarcinomas, *PNM* pancreatic neck margin, *PP* partial pancreatectomy, *SMAM* superior mesenteric artery margin, *SP* subtotal pancreatectomy, *TP* total pancreatectomy
[a]Luminal margins (proximal gastric or duodenal and distal jejunal) are considered as two different margins
[b]R1 and R2 resections are included

As previously seen, it has been demonstrated that R1 rate increases significantly (>75%) and correlates with survival after exhaustive and meticulous standardized pathological examination [17, 18, 21–26]. In consequence, a high rate of R1 resections is an indicator of high-quality pathology more than a low-quality surgery [18, 61]. These conclusions have focused the attention to pathology aspects related to specimen handling and reporting [37].

In addition to the lack of consensus on margin terminology and slicing techniques, R1 definition is also controversial. While a positive margin (R1) is understood for the majority of North American pathologists and their guidelines only when the tumor is directly in contact with the inked margin (0 mm clearance) [13, 31, 40, 41, 46, 77], for European and Australian pathologists, R1 margin involvement is defined as tumor within 1 mm of the margin (the distance to the resection margin is 1 mm or less) with the exception to anterior surface [17, 18, 30, 38, 39]. This "1 mm rule" was extrapolated

from the R1 definition of rectal cancer assessment [17, 38], but it has never been validated in pancreatic cancer [64]. A 0 mm clearance definition could be valid for tumors whose growth pattern is compact. However, in PDCA it is characterized by an infiltrative growth pattern. According to the study of Verbeke and colleagues [64], pancreatic cancer, including PDCA, DBDC, and ampullary carcinomas, shows a higher dispersed growth pattern of tumor cells when compared to rectal cancer, especially on the edge. This means that a 0 mm clearance does not guarantee complete resection [78]. In fact even ≤1 mm could be insufficient in pancreatic cancer [64]. It has been recently suggested that a cutoff of 1.5 mm could be clinically more significant [15, 47].

Another important issue is the relevance of the type of tumor spread at the margin. Apart from the primary tumor mass (direct invasion), the presence of tumor cells in the vascular, lymphatic, or perineural spaces or within lymph nodes could also be considered as margin involvement (indirect invasion) [20]. In the residual tumor (R) classification included in the TNM system of the IUCC/AJCC, some "special situations" are explained [79]. This classification considers R1 resection when tumor cells are attached to or invade the vessel walls at the margin. Despite the absence of clearer evidence, the RCPUK [38] protocol and the RCPA [39] protocol suggest considering R1 resection in cases of indirect invasion, but it should be clearly stated in the report. In any case, the isolated margin involved by indirect invasion with no direct invasion at any other point is extremely rare [18, 61].

26.2.4 Lymph Node Metastases: The Magic Number

Lymph node (LN) involvement has been considered an adverse prognosis factor in pancreatic carcinoma [13, 80–85]. The number of LN evaluated has been related to patients' outcome by some authors [86–88]. However, others did not demonstrate this relation [89, 90]. The minimum number of LN required in a CDP for considering optimal staging varies from 12 [39, 41, 86] to 15 [38, 40, 87, 91], and it is considered a good indicator of the quality of both the surgical procedure and pathologic handling. It must be taken into consideration that fewer lymph nodes may be identified after neoadjuvant treatment [39]. Another number has also been described: the "lymph node ratio" (LNR) defined as the ratio between metastatic and evaluated/retrieved LN, which is directly related to survival and considered a new major clinical predictor even more powerful than the overall nodal status in resected pancreatic cancer [86, 88, 92–96]. However, a recent paper suggests that only the presence of lymph node metastasis is of prognostic value, regardless the number of positive nodes or the LNR [89].

26.3 Pathology Report of Pancreatic Cancer Specimens: Cephalic Duodenopancreatectomies and Distal and Total Pancreatectomies

An ideal protocol for reporting pancreatic cancer specimens must be easily applicable and accurate, well understood by other clinicians, and useful in assessing relevant information for planning treatment and establishing prognosis. It is very important for pathologists and clinicians to "speak the same language." Protocols are available in the literature and ready for use [38–40]. However, disagreements in some basic concepts raise doubts in pathology communities; in addition, some aspects are superficially described or incompletely developed (e.g., tumor banking is only included in the RCPA protocol).

The best way to approach a pancreatic head resection specimen in order to assure accurate assessment of all previously relevant described parameters is likely to be axial slicing with wide sampling. To date, no general consensus among pathologists has been reached, and consequently the final decision continues to be the pathologist's best opinion.

26.3.1 Specimen Orientation, Inking Margins, and Slicing

In this section a practical and easy few-step guide for the macroscopic handling of pancreatic specimens based on the axial slicing technique [17, 18, 38] is developed. The collaboration of the surgeon for handling the pancreatic specimen is recommended until familiarity is achieved.

1. The first step is to check the identification number and patient data. With the fresh specimen, identify the type of surgical specimen, CDP, distal pancreatectomy (DP), or total pancreatectomy (TP), and check if any preoperative treatment was performed.
2. In CDP specimens, identify margins. Gastroduodenal margins and biliary duct margin are easily found from the anterior view (Fig. 26.1). The anterior surface is also seen. The pancreatic neck margin (PNM) is observed from the posterior view, where the SMVM, SMAM, and posterior margin are also identifiable (Fig. 26.2). Notice if any segment of vessel is included (more likely in specimen post therapy).
3. Open the lumen by cutting through the antimesenteric border of the duodenum, and analyze the gastrointestinal lumen in order to identify any possible tumor lesion in the ampulla of Vater. If not, explore the specimen so as to locate the tumor. When a PDAC or DBDC is suspected, SMVM concavity is usually very distinct.
4. If fresh tissue is to be taken for banking, all margins must be inked in different colors before partially cutting the specimen. If not, margin inking can be carried out after fixation.
5. The specimen must be left at least 24–48 h in formaldehyde to allow correct fixation and guarantee good consistency to make slices.
6. Ink margins in different colors: PNM, SMVM, SMAM, and posterior margin. If a vascular segment is included, it must be inked in a different color. Anterior surface is also recommended to be inked (Fig. 26.4).
7. Take gastrointestinal margins and BDM en face (Fig. 26.5a–c). PNM can also be taken by shaving (Fig. 26.5d). PNM has usually been studied during intraoperative assessment, so it is supposed to be free in the pancreatic specimen with a distance to the margin of more than 1 mm (pancreatic slice for intraoperative study is 2–3 mm thick). If PNM has not been previously studied, it could be left in the specimen in order to take perpendicular sections for measuring the distance to the tumor.
8. Make the first slice in a plane perpendicular to the longitudinal axis of the duodenum through the middle of the ampulla de Vater (Fig. 26.6a), and continue slicing in parallel sections to both directions with a thickness of 5 mm more or less. Several slices will be produced (Fig. 26.6b).
9. Identify the tumor, measure it, and study the relations to structures and macroscopic distance to the margins. These sections can easily be compared with previous image studies (Fig. 26.7).
10. Take representative samples of the tumor in relation to all the margins and structures (Fig. 26.8). If macroscopic tumor cannot be identified, as in some cases with neoadjuvant therapy, consider total inclusion from the beginning to avoid resampling.
11. Take a sample from the ampulla, from the nonneoplastic pancreas and from any other lesion identified.
12. Identify lymph nodes from the different stations for individual analysis. LNs are recommended to be embedded completely unless macroscopic involvement is evident (in which case only one block or section is required) [39].
13. In DP specimens, the procedure is the same. Ink the margins: pancreatic transection margin (similar to PNM) and anterior and posterior surface of the tail. The spleen is normally included in these specimens. Slice en face section of the pancreatic transection margin, and continue slicing the specimen perpendicular to the tail long axis (Fig. 26.9). Take samples of the tumor in relation to margins and vascular structures; take also representative samples of the spleen. Identify lymph nodes from the different stations for individual analysis.

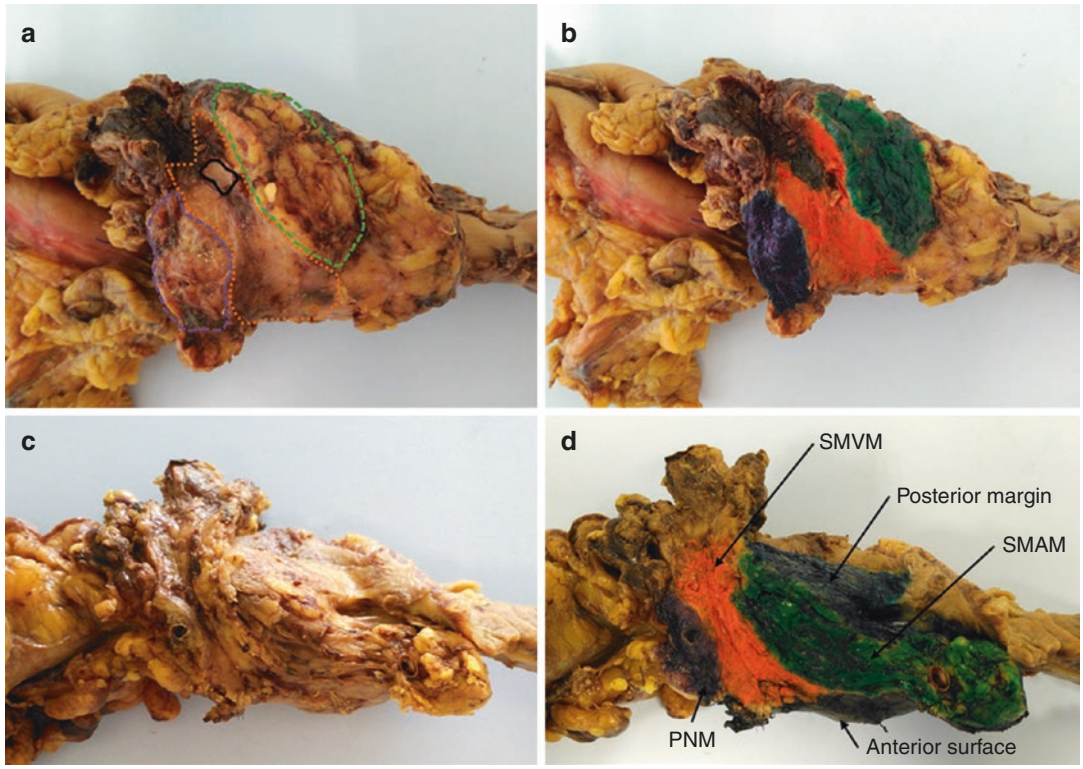

Fig. 26.4 (**a**) CDP specimen including a segment of vein. PNM, SMVM, and SMAM are delineated by *discontinuous violet, orange*, and *green lines*, respectively. Vascular segment is highlighted demarcated by a *black line*. (**b**) The same specimen after inking margins. (**c**, **d**) Another CDP specimen before and after inking. All margins and surfaces are inked with the following color code: *violet* for PNM, SMVM in *orange*, SMAM in *green*, *black* for anterior surface, and posterior margin in *blue*

14. In TP specimens, ink anterior surface, SMVM, SMAM, and posterior margin of the head and anterior and posterior surface of the body-tail. Include gastroduodenal margins and BDM. PNM is logically not present in these specimens (Fig. 26.10). Split the specimen into head and body-tail, and proceed as seen before. Lymph nodes sampling as usual.

26.3.2 Microscopic Examination and Pathologic Reporting

Some data that need to be addressed in pathology reporting are the following:

- Tumor location and histological subtype and grade are assessed according to the latest version of the World Health Organization (WHO) classification [97] (Appendixes 1 and 2).
- Tumor size and extension (invasion to adipose tissue, duodenum muscular wall, or other organs) are also recorded (Fig. 26.11a).
- Perineural and lymphovascular invasion have been shown to be adverse prognostic factors and should also be reported [85] (Fig. 26.11b, c).
- The regional lymph nodes for the pancreatic and periampullary carcinomas can be grouped according to AJCC or the JPS (Fig. 26.12) [41, 56] (Appendix 3). All lymph nodes should be examined histologically (Fig. 26.11d), specifying the area if possible. Direct extension to the primary tumor into a lymph node is considered lymph node metastasis according to the AJCC 7th edition [98]. According to RCPUK protocol [38], the use of immunohistochemistry to detect micrometastases is not still recommended in daily practice even though it has been demonstrated in one study that detection of isolated tumor cells or small clusters of cells

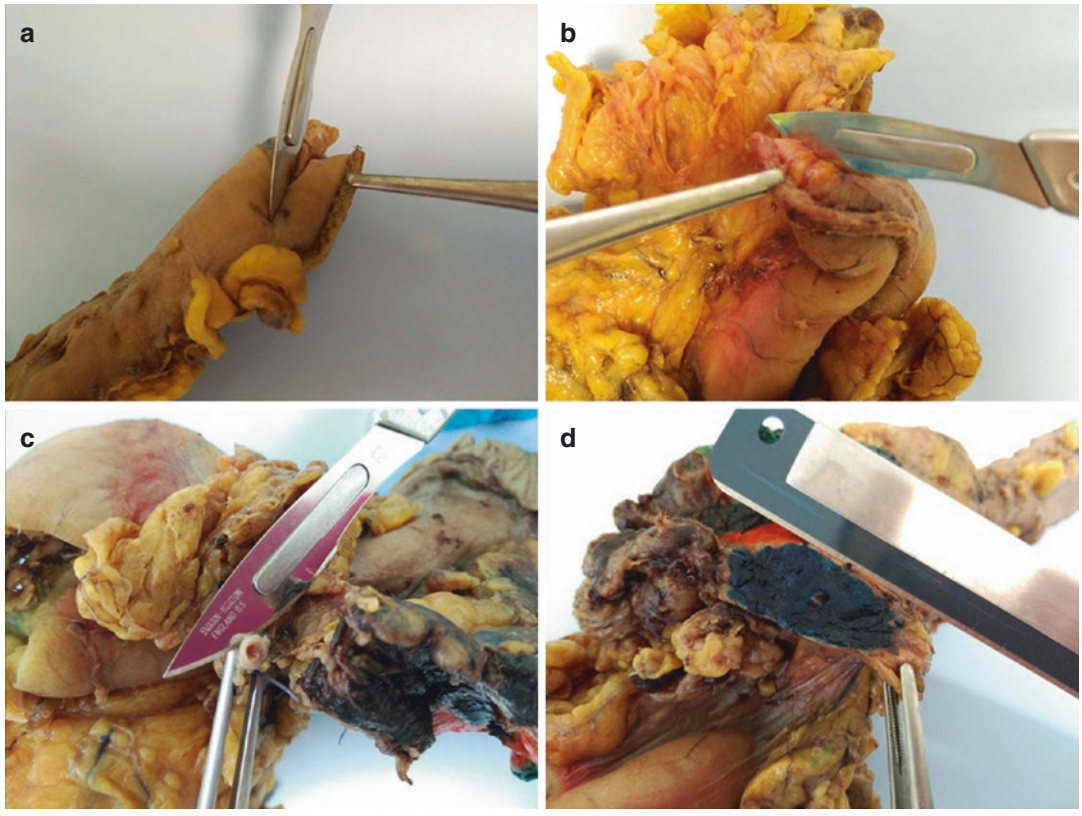

Fig. 26.5 Different margins taken by en face technique. (**a**) Duodenal distal margin. (**b**) Gastric proximal margin. (**c**) BDM. (**d**) PNM

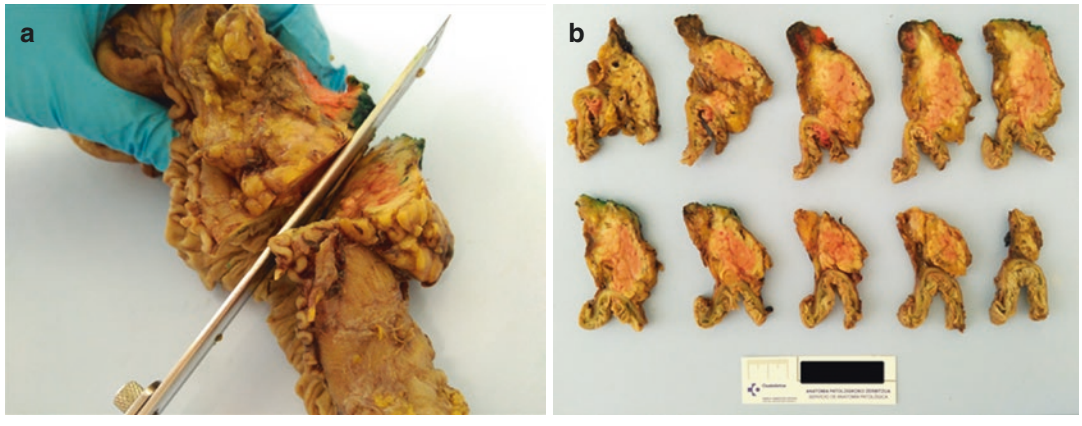

Fig. 26.6 (**a**) First slice through the ampulla of Vater, perpendicular to the duodenal axe (axial technique). (**b**) 3–5 mm thick consecutive slices of the complete specimen

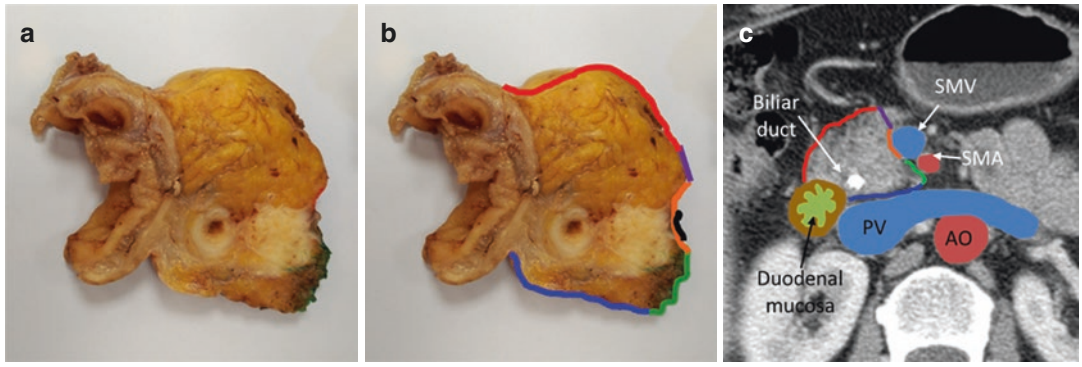

Fig. 26.7 (**a**) A selected section. (**b**) Schematic representation of all margins in the same photograph (*blue*, posterior margin; *green*, SMAM; *orange*, SMVM; *black*, vascular segment; *violet*, PNM; and *red*, anterior surface). (**c**) The same color code as in picture **b** is represented in the scanner image. Duodenal mucosa and vasculature are also colored in the scanner image: superior mesenteric vein (SMV), superior mesenteric artery (SMA), portal vein (PV), and aorta (AO). Bile duct is recognized by the presence of prosthesis

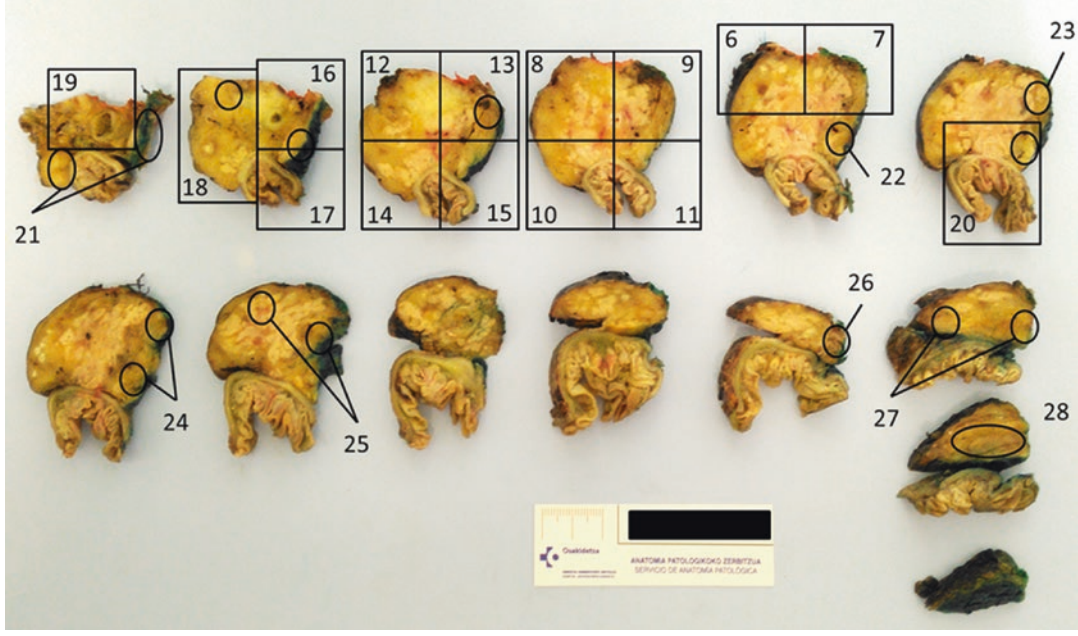

Fig. 26.8 Photograph of the complete sliced specimen where schema of tumor samples is written down. The vast majority of tumor is taken as well as the ampulla (number 20) and lymph nodes (*circles*), some of them with inked margin (numbers 21–28)

by immunohistochemistry in lymph nodes is an independent adverse prognostic factor in PDCA staged as N0 [99].

– Microscopic distance to every margin should be reported, especially if less than 1–1.5 mm. When a segment of vascular channel is included, identify the level of invasion with the wall, and look for tumor cells in the luminal side (Fig. 26.13).
– Response to neoadjuvant therapy should be also evaluated (see next section).
– Precursor lesions are frequent on the adjacent pancreas and need to be stated. The problematic issue is their significance at the margins.

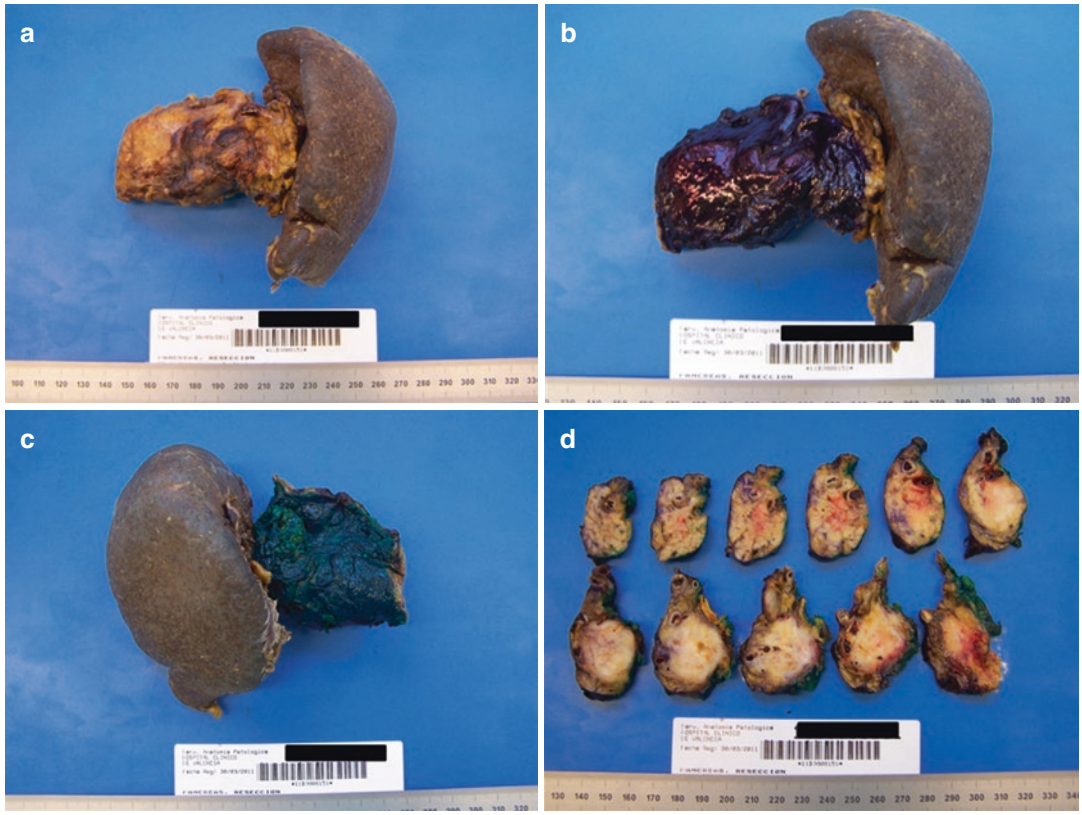

Fig. 26.9 Distal pancreatectomy (DP) specimen. (**a**) Anterior view. (**b**) Anterior margin inked in *violet*. (**c**) Posterior margin in *green color*. (**d**) Consecutive slices from pancreatic margin (*the upper left corner*) to the end of the tail (*the lower right corner*)

Although the significance of low-grade PanIN is uncertain because it can be also found in the context of benign lesions, reporting PanIN-3 at the margins is generally recommended [38–40].

An example of a straightforward template for pathologic reporting of the pancreatic and periampullary cancer specimen is proposed in which all of this data is included (Appendix 4).

26.3.3 Pathological Staging in Pancreatic Cancer

As in other solid neoplasms, the staging of patients at diagnosis should provide one of the strongest prognostic factors of outcome in their specific tumor type. The TNM classification developed by the AJCC [98] is a worldwide accepted cancer staging system, based on three characteristics: tumor size/extent of the disease (T), lymph node spread (N), and the presence of distant metastases (M). The principles for creating a staging system in a particular malignancy are few: individual staging should stratify patients into prognostic groups with statistically significant differences among them which are clinically relevant; the system needs to be reproducible and easily incorporated into general practice [100].

In the particular case of pancreatic cancer, some of the pathology staging parameters included in the seventh edition were difficult to apply in routine practice according to some international experts [101]. For that reason, some major changes for T and N classification have

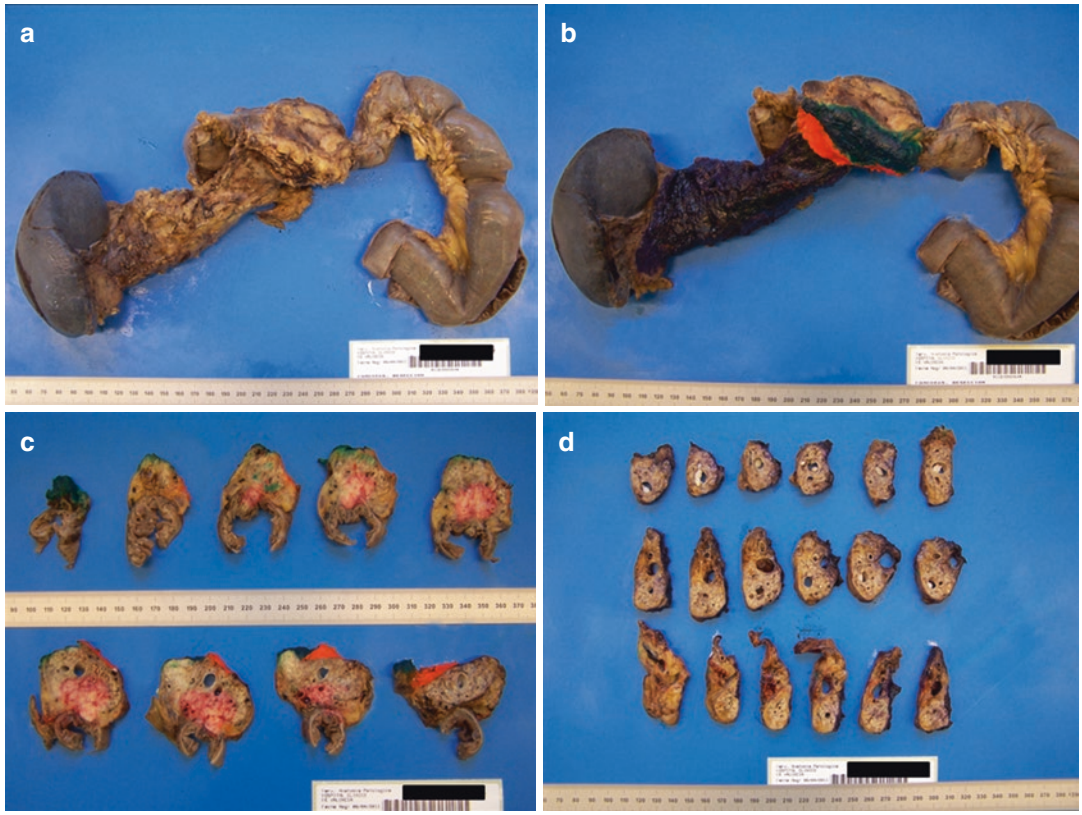

Fig. 26.10 Total pancreatectomy (TP) specimen. (**a**) Posterior view. (**b**) Posterior view after inking with the following color code: *violet* for complete posterior surface, *orange* for SMVM, and *green* for SMAM. Anterior surface and posterior margin are not inked in the photograph. (**c**, **d**) Consecutive slices corresponding to the head of the pancreas (**c**) and to the body-tail (**d**). The whole specimen is full of cystic spaces

been proposed for the next eight edition of the TNM [100] (Appendix 5). These changes have been explored in 2318 patients, and the results were statistically valid and allowed a more reproducible system, especially in T staging. This new system, according to the authors, also stratifies patients more evenly across stages without sacrificing prognostic accuracy [100]. However, this classification does not include some important prognostic factors for pancreatic and periampullary carcinomas such us margin involvement or response to neoadjuvant therapy.

26.4 Role of Frozen Section During Surgery for Pancreatic/Periampullary Cancer

Intraoperative examination by frozen sections is commonly performed for pancreatic surgery in order to obtain histological diagnosis when only clinical suspicion is available, to assess resectability in the case of unexpected locoregional spread, and to ensure free margins [102].

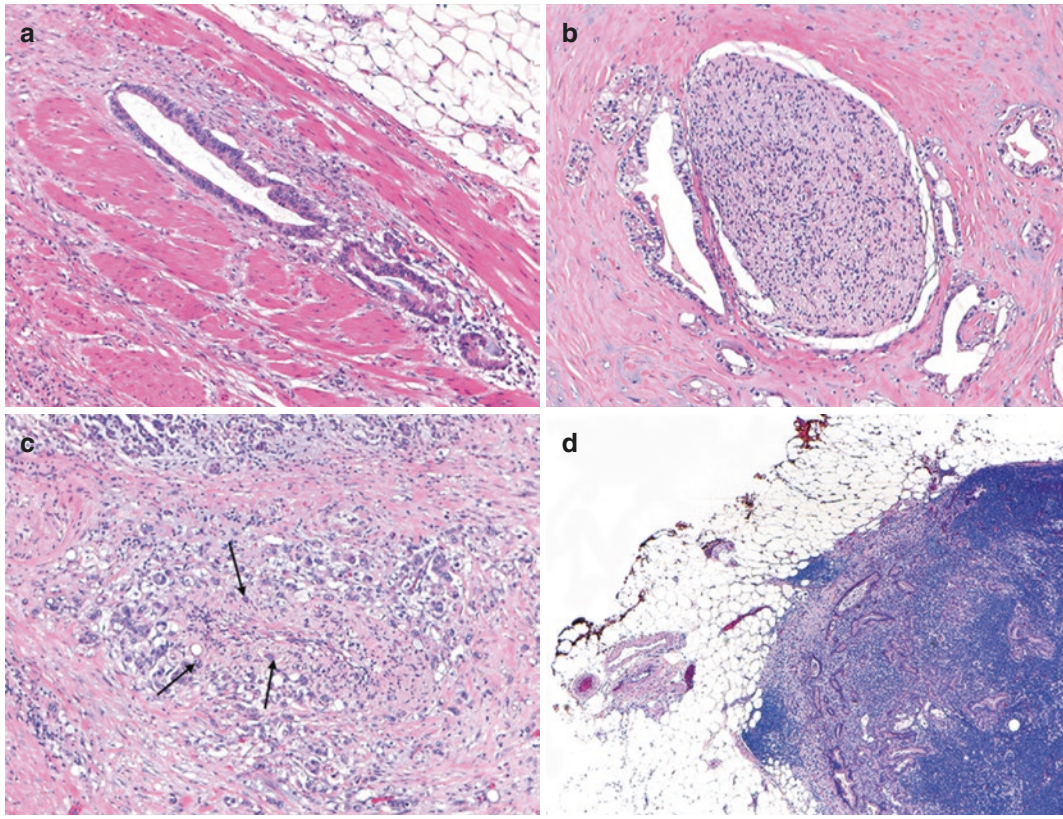

Fig. 26.11 Microscopic details of a pancreatic adenocarcinoma. (**a**) Invasion of the muscular wall of the duodenum, (**b**) perineural invasion, (**c**) vascular invasion (*arrows*, tumor cell permeating the vessel wall), and (**d**) a metastatic lymph node close to the inked margin (H&E, 100× magnification)

Intraoperative studies for confirmation of malignancy are less frequent nowadays. The incidence of false-negative results varies in the published literature from 1.2% to 75% [102–104]. The improvement of diagnostic imaging tools such as high-resolution multislice spiral CT allows the diagnosis of malignancy in the majority of cases (97%), and even resectability could be assessed with high accuracy [105]. In addition to this, the use of minimal invasive techniques such as EUS-FNA, which can diagnose cancer with a 90% sensibility and a 100% specificity in expert cytopathologist hands [106], may drastically reduce the number of patients entering the operating room with no previous diagnosis.

For the assessment of locoregional spread, frozen sections can be performed in any incidental finding during surgery (hepatic, peritoneal lesions or suspicious para-aortic lymph nodes), which were not identified on routine imaging.

Pancreatic cancer surgery aims to achieve R0 resections. Frozen sections allow further resection if a positive margin is found and therefore increase the rate of final R0 [54, 107]. However, the impact of microscopic involvement of margins seems to be less critical than the presence of micrometastatic disease, biology aggressiveness, or lymph node metastases [77], which is why intraoperative margin assessment during pancreatic surgery for achieving usefulness R0 resec-

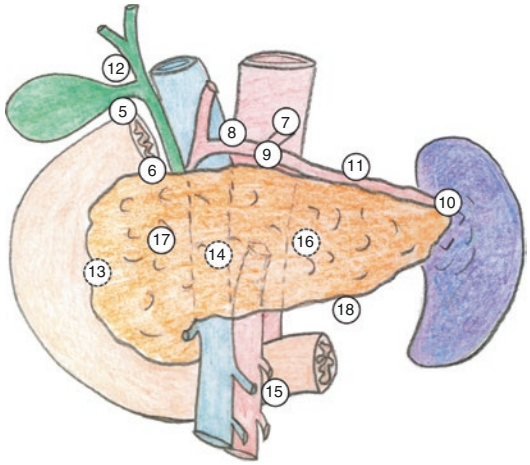

Fig. 26.12 Schematic design of the Japan Pancreas Society node stations [56]

tion has been a matter of debate over the last years.

Regarding which margins should be evaluated intraoperatively, the most important margins are, logically, vascular (SMVM and SMAM) and posterior due to their high rate of involvement. However, even if one of these margins is positive intraoperatively, an extended resection at this level is impossible. For that reason an "artery-first" surgical approach is defended by some groups in order to reduce the number of R1 resections, but the benefit seems to be limited [108–113].

BDM frequently requires intraoperative examination, more important when origin in biliary tract is suspected.

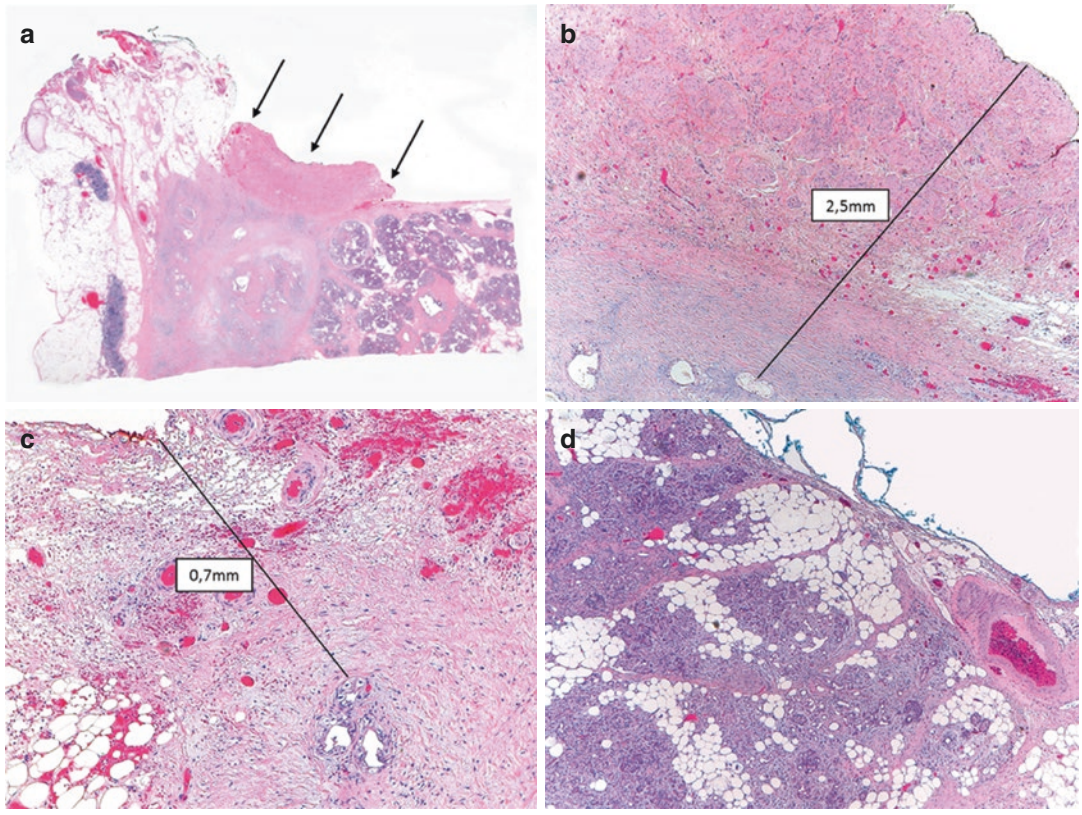

Fig. 26.13 (**a**) Panoramic view of a pancreatic section including SMVM and SMVM. A portion of vessel is attached to SMVM (*arrows*). From this magnification, the tumor area is distinguished from pancreatic parenchyma and adipose tissue (stars) (H&E, 10× magnification). (**b**) High-power field of vessel margin. Tumor gland is more than 2 mm far away from the lumen, and no wall invasion is seen (H&E, 40× magnification). (**c**) Tumor gland within the 1 mm of the margin. This is considered R1 resection for many authors (H&E, 40× magnification). (**d**) Inked margin in *green color*. No tumor is identified within 1 mm (H&E, 40× magnification)

Table 26.4 Comparison of grading systems of pathologic response to neoadjuvant therapy in pancreatic cancer reported in the literature

Authors	Year	Grades	Histologic criteria	Description
Ishikawa et al. [138]	1989	3	SDCC: Severely degenerated cancer cells	1: <33% severely degenerated cancer cells 2: 33–66% degenerated cancer cells 3: ≥66% degenerated cancer cells
Evans et al. [132]	1992	4	Viability	I. Characteristic cytologic changes of malignancy are present, but little (<10%) or no tumor cell destruction is evident II. In addition to characteristic cytologic changes of malignancy, 10–90% of tumor cells are destroyed IIa. Destruction of 10–50% of tumor cells IIb. Destruction of 51–90% of tumor cells III. Few (<10%) viable-appearing tumor cell are present IIIM. Sizable pools of mucin are present IV. No viable tumor cells are present IVM. Acellular pools of mucin are present
Pendurthi et al. [139]	1996	2	Fibrosis	<80% fibrosis ≥80% fibrosis
White et al. [137]	2005	4	Necrosis, residual tumor load, and fibrosis	*Necrosis*: Extensive / Moderate / Focal / Absent *Residual tumor load*: Large / Moderate / Small / Minimal / None *Fibrosis*: Extensive / Moderate / Mild
Chun et al. [125]	2011	3	Fibrosis	– Minor: <50% fibrosis relative to residual neoplastic cells – Partial: 50 ≤ fibrosis < 95% – Major: ≥95% fibrosis
Hartman and Krasinskas [129]	2012	3/4	Necrosis, residual tumor load, and fibrosis	– Poor: No definite evidence of treatment effect; extensive (>90%) residual cancer; only minimal cytopathic effect and baseline fibrosis are present – Minimal to moderate: Residual tumor present; includes small groups of cells/glands without evidence of cytopathic effect, cells/glands outside the main fibrotic mass, and/or >5% of the main fibrotic mass with cancer/glands, with or without cytopathic effect – Marked response: No residual tumor or rare, single cancer cells or small groups of cancer cells (glands) with marked cytopathic effect present with a fibrotic stroma *the presence of necrosis is reported separately **if no tumor cells are identified within a lesion that was submitted in its entirety for histologic examination, then the designation complete response can be rendered
Chatterjee et al. [140] and Verbeke et al. [133]	2012, 2015	2	Residual tumor	– Complete or near-complete response (single cells or small groups of cancer cells) – Limited or no response
CAP and RCPA [Ryan system] [39, 40, 136]	2005, 2014, 2016	4	Residual tumor, fibrosis	0 (complete response): no viable tumoral cells 1 (moderate response): single cells or small groups of tumoral cells 2 (minimal response): residual tumor with fibrosis 3 (poor): extensive residual tumor

CAP College of American Pathologists, *RCPA* Royal College of Pathologists of Australasia

Concerning the pancreatic neck margin (PNM), controversy is open for debate. R0 PNM resection has proved to be prognostic [114]. Achieving a negative PNM after a positive result during intraoperative assessment can be reached by taking an additional pancreatic slice or performing a total pancreatectomy. However, the real value in terms of survival of extended surgery is not totally clear [37]. While some institutions have shown an improvement in overall survival [70, 115], other studies have not demonstrated any survival benefit [54, 107, 116, 117]. Although the prognostic significance of extended surgery is in doubt and could be of limited benefit, intraoperative analysis still remains a current practice in many hospitals [54]. This is explained by the fact that a complete R0 surgery is thought to be the best chance to improve outcome but only if extended surgery does not increase morbidity.

Regarding precursor lesions of pancreatic cancer (PanIN and IPMN), there are some general agreements in their intraoperative examination on resection margins [118, 119]. It has been demonstrated that the presence of PanIN of any grade at the margin during surgical resection for pancreatic cancer does not influence in terms of survival [120]. However, the presence of a high-grade PanIN is highly suggestive of near invasive carcinoma and should imply further surgery [121]. In cases of IPMN, only high-grade or invasive carcinoma is required to be reported for more extensive surgery [118]. The presence of low-grade dysplasia at the margin does not justify extended surgery for now [120, 122, 123].

Frozen section diagnosis is often a challenge for pathologists who need to render a diagnosis with critical implication for the patient in a very short time and on a small piece of frozen tissue with the consequent artifacts and potential pitfalls (Fig. 26.14). Chronic pancreatitis and other inflammatory changes are the most commonly difficult differential diagnoses in pancreatic frozen sections. In cases of IPMN, denuded epithaelium should also be reported because of the impossibility for assessing malignancy [118,

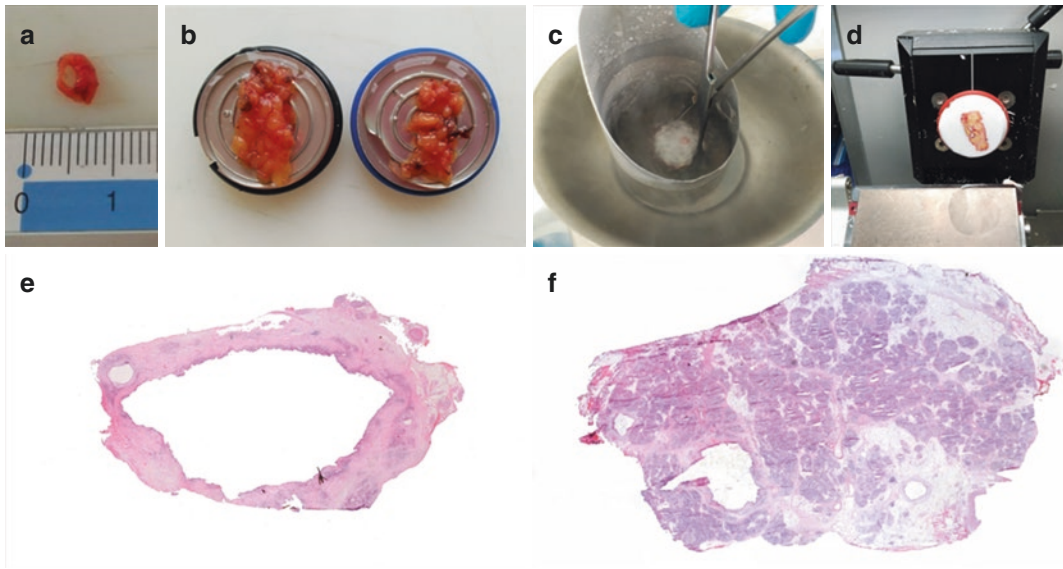

Fig. 26.14 Images of an intraoperative assessment. (**a**) One of the samples usually asked intraoperatively (BDM). (**b**) Distant suspicious lymph nodes can also be sent. Specimens are put in a special platform with OCT. (**c**) Frozen process in liquid nitrogen. (**d**) Cutting process is followed by staining in H&E. (**f**, **g**) Panoramic view of frozen sections corresponding to BDM and PNM, respectively (H&E, 10× magnification)

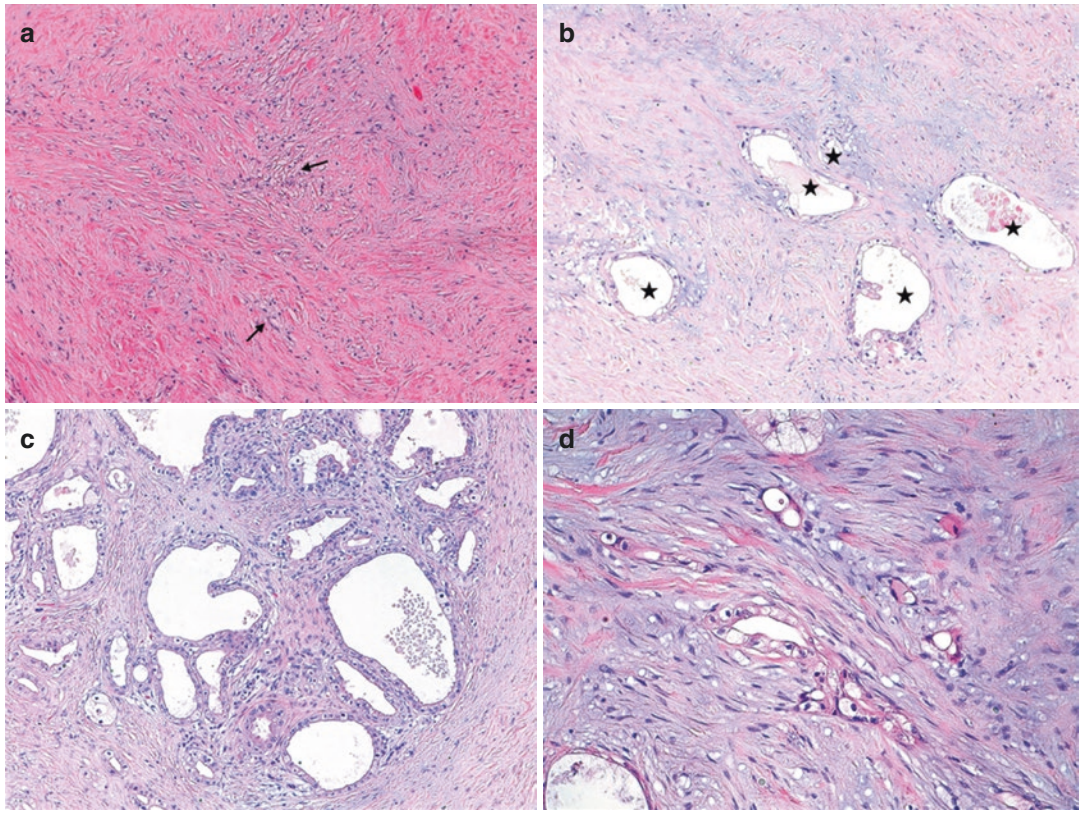

Fig. 26.15 Microscopic view of post-treatment specimen. (**a**) Isolated cells (*arrows*) within fibromyxoid matrix (H&E, 100× magnification). (**b**) Scattered tumor glands (*stars*) (H&E, 100× magnification). (**c**) Predominance of residual tumor cells over fibrosis (H&E, 100× magnification). (**d**) Detail of tumor cells. Cytologic changes include clear and eosinophilic cytoplasm and pyknotic appearance of the nucleus (H&E, 200× magnification)

124]. Moreover the distinction between low- and high-grade lesions is often quite difficult, and sometimes it is not possible to confidently exclude the presence of invasive carcinoma/high-grade dysplasia during intraoperative assessment [118].

26.5 Assessment of the Histopathological Response After Neoadjuvant Therapy

Pathological response to neoadjuvant therapy is an important prognostic factor in many other tumors. However, the relevance of pathological response in pancreatic cancer survival still remains unclear [125–127].

Preoperative chemoradiation is being used on borderline or non-resectable patients in an attempt to offer at least a percentage of these patients a surgical approach [125]. Nowadays more and more patients are being treated with neoadjuvant chemoradiation, even if they are initially resectable. The intention is to ameliorate such poor results in margin involvement rates and patient survival when dealing with tumors thought to be locally restricted [128–130]. Indeed, adjuvant chemotherapy after surgery is not performed in at least a quarter of patients due to the prolonged recovery of this aggressive surgery [131]. Summarizing, some of the claims in favor of neoadjuvant chemoradiation therapy are to avoid surgery in very aggressive tumors which rapidly progress despite treatment, to provide more effective chemotherapy in an unaltered and

well-vascularized tumor, to reduce secondary effects and improve tolerance of the treatment in a healthier patient (before surgery), to evaluate its effectiveness, to improve the rate of negative surgical margins, and to provide an early treatment of any possible occult micrometastases [125, 128, 132, 133].

This increase of pretreated patients means that many of the pancreatic specimens will need evaluation for histopathological response of treatment. However, a consensus for the reporting criteria is lacking [125, 133].

Pancreatic cancer is a very challenging neoplasm, and the assessment of pathological therapy response is as complicated as other aspects of these tumors. The first obstacle is to differentiate the effect of chemoradiation in terms of morphology from untreated tumors (Fig. 26.15). Indeed, the vast majority of patients are diagnosed by fine needle aspiration where architecture and other parameters such us fibrosis or necrosis cannot be compared with the histology of the specimen. The second problem is defining which parameters to consider for evaluating pathological response. Assessing the amount of fibrosis due to posttreatment effect in a tumor where the main morphological feature is fibrosis is quite difficult and subjective. Finally, the grading system must be feasible and reproducible. The more grades the system has, the more accurate it is expected to be, but it becomes extremely complex and less efficient in the end.

Many schemas have been described in other neoplasms of the gastrointestinal tract such as rectal or esophageal cancer [134–136], perhaps due to the widespread use of neoadjuvant treatment. Few articles referring specifically to histologic grading of treatment response in pancreatic ductal adenocarcinoma have been published [125, 129, 132, 133, 137–140], and none of them have been completely accepted. In fact, the CAP recommends in its protocol [40] the assessment of the therapy response by a four-tiered system based on one by Ryan et al. [136]. This scheme was originally used for rectal cancers with neoadjuvant therapy and perhaps, as pointed out by Hartman and Krasinskas [129], probably recommended with the intention of homogenizing pathology reports of gastrointestinal cancers. The protocol also manifests that other systems can be used but any reference of specific protocols for pancreatic cancer is referred. The RCPA also uses the same grade system in its protocol [39], but any reference to reporting treatment effect is addressed on RCPUK protocol [38]. In Table 26.4 the different systems for grading therapy effect in pancreatic cancer specimens are compared.

Ishikawa et al. [138] proposed a three-tiered grading system based on the percentage of the concept SDCC (severely degenerated cancer cells). The Evans system [132] defined four grades (with respective subgrades) assessing the percentage of destruction of tumor cells. Pendruthi et al. [139] divided patients in two grades depending on fibrosis. White et al. [137], similarly to Evans, proposed a three-tiered grading system based on the percentage of residual tumor in addition to necrosis and fibrosis. Chun et al. [125] positioned their classification based exclusively on fibrosis in three grades. The study of Hartman and Krasinskas [129] is a very exhaustive and critical review of the different previous proposed grading systems of pretreated pancreatic cancers. These authors analyze in depth each criterion used for grading and their advantages and limitations; they conclude that routine hematoxylin-eosin stained sections are the only method to assess histopathological response to treatment at present, emphasizing on the importance of sampling correct methodology. Their so-called simplified three-tiered system is a modification of the scheme proposed by the CAP with the admixture of some ideas or concepts of Ishikawa et al. [138] and Evans et al. [132] grading systems.

It is true that the four-tiered system based on residual tumor cells and fibrosis proposed by the CAP protocol is widely used. This system avoids subjective histomorphology concepts like “viable tumor cell,” and it is likely to reduce intra-

observer and interobserver variability. As proposed by Hartman and Krasinskas [129], the use of a complementary description is a perfect idea to avoid any confusion. However, considering that only complete response seems to be related to improved survival, other authors claim a more simple and pragmatic system with two grades: complete or near-complete response (single cells or small groups of cancer cells) and limited or no response [133, 140].

In addition to the response evaluation, many other issues regarding posttreatment specimens have still not been addressed [133]. International consensus is urgently needed regarding not only pathologic response but also macroscopic examination. While some questions remain unsolved, such us whether 1 mm margin clearance is enough in pre-treated specimens or if it is necessary pathological evaluation of regression in lymph nodes in routinely practice, some practical recommendations are addressed by Verbeke et al. [133].

Conclusion

At present, pathology reporting in pancreatic and periampullary neoplasms remains one of the main pillars in patient care, and it highly influences therapeutic decisions. It has been thoroughly demonstrated that pancreatic specimens are complex, and a meticulous standardized protocol is the only option to obtain reliable data and to guarantee comparable results among studies. We propose a handling and reporting protocol based on the published literature of the main international groups. However, an international consensus in basic and controversial pathology aspects is urgently required.

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Appendix 1: WHO Classification of Malignant Epithelial Tumors of the Pancreas, Gallbladder and Extrahepatic Bile Ducts, Ampulla Region, and Small Intestine [97]

Pancreas
- Ductal adenocarcinoma
  - Adenosquamous carcinoma
  - Colloid carcinoma (mucinous noncystic carcinoma)
  - Hepatoid carcinoma
  - Medullary carcinoma
  - Signet ring cell carcinoma
  - Undifferentiated (anaplastic) carcinoma
  - Undifferentiated carcinoma with osteoclast-like giant cells
- Acinar cell carcinoma
- Acinar cell cystadenocarcinoma
- Intraductal papillary-mucinous neoplasm with an associated invasive carcinoma
- Mixed acinar-ductal carcinoma
- Mixed acinar-neuroendocrine carcinoma
- Mixed acinar-neuroendocrine-ductal carcinoma
- Mixed ductal-neuroendocrine carcinoma
- Mucinous cystic neoplasm with an associated invasive carcinoma
- Pancreatoblastoma
- Serous cystadenocarcinoma
- Solid-pseudopapillary neoplasm

Gallbladder and extrahepatic bile ducts
- Adenocarcinoma
  - Adenocarcinoma, biliary type
  - Adenocarcinoma, gastric foveolar type
  - Adenocarcinoma, intestinal type
  - Clear cell adenocarcinoma
  - Mucinous adenocarcinoma
  - Signet ring cell carcinoma
- Adenosquamous carcinoma
- Intracystic (gallbladder) or intraductal (bile ducts) papillary neoplasm with an associated invasive carcinoma
- Mucinous cystic neoplasm with an associated invasive carcinoma
- Squamous cell carcinoma
- Undifferentiated carcinoma small intestine

Ampullary region
- Adenocarcinoma
  - Invasive intestinal type
  - Pancreatobiliary type
- Adenosquamous carcinoma
- Clear cell carcinoma
- Hepatoid adenocarcinoma
- Invasive papillary adenocarcinoma
- Mucinous adenocarcinoma
- Signet ring cell carcinoma
- Squamous cell carcinoma
- Undifferentiated carcinoma
- Undifferentiated carcinoma with osteoclast-like giant cells

Small intestine
- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet ring cell carcinoma
- Adenosquamous carcinoma
- Medullary carcinoma
- Squamous cell carcinoma
- Undifferentiated carcinoma

Benign and premalignant epithelial lesions and neuroendocrine tumors are not included

Appendix 2: Histopathological Grading of PDAC According to WHO Classification [97, 141]

Tumor grade	Glandular differentiation	Mucin production	Mitoses (per 10 HPF)	Nuclear features
Grade 1	Well differentiated	Intensive	5	Little polymorphism, polar arrangement
Grade 2	Moderately differentiated duct-like structures and tubular glands	Irregular	6–10	Moderate polymorphism
Grade 3	Poorly differentiated glands, abortive mucoepidermoid and pleomorphic structures	Abortive	>10	Marked polymorphism and increased size

HPF high-power field

Appendix 3: Equivalences Between Lymph Node Stations According to JPS and AJCC-UICC Classification [41, 56]

JPS node stations	UICC node stations
5	Suprapyloric
6	Infrapyloric
7	Left gastric artery
8	Common hepatic artery
9	Celiac
10	Splenic hilum
11	Superior splenic artery
12	Hepatoduodenal ligament (portal/bile duct)
13	Posterior pancreaticoduodenal
14	Superior mesenteric vessel
15	Colic artery
16	Para-aortic
17	Anterior pancreaticoduodenal
18	Inferior

Appendix 4: Example of Pathologic Report of the Pancreatic and Periampullary Cancer Specimens

<table>
<tr><td colspan="3">Pathologic report of pancreatic specimens</td></tr>
<tr><td>Patient:
– Name:
– Age:
– Affiliation number:</td><td colspan="2">Identification number:
Tumor banking: Yes no</td></tr>
<tr><td>Previous diagnosis:</td><td colspan="2">Photodocumentation: Yes no</td></tr>
<tr><td colspan="3">Macroscopic examination</td></tr>
<tr><td>Specimen type:</td><td colspan="2">Tumor location:</td></tr>
<tr><td>Macroscopic characteristics:</td><td colspan="2">Tumor size: cm</td></tr>
<tr><td colspan="3">Microscopic examination</td></tr>
<tr><td>Histologic type:</td><td rowspan="3">Invasion:
– Vascular
– Lymphatic
– Perineural</td><td rowspan="3">Precursor lesions:
– PanIN
– IPMN
– Other:</td></tr>
<tr><td>Histologic grade:</td></tr>
<tr><td>Microscopic tumor size: cm</td></tr>
</table>

Pathologic report of pancreatic specimens			
Tumor extension: **Treatment effect (neoadjuvant therapy):** – Complete response (grade 0) – Moderate response (grade 1) – Minimal response (grade 2) – Poor response (grade 3)	**Nonneoplastic lesions** – Bile duct obstruction – Pancreatic duct obstruction – Pancreatic calculi – Chronic pancreatitis – Other:		
Margins distance*:	**Lymph nodes:**	+	Total
– Proximal (luminal): – Distal (luminal): – CBD: – PNM: – Anterior surface: – Posterior margin: – SMVM: – SMAM: – Other:	– Suprapyloric (S5)		
	– Infrapyloric (S6)		
	– Peripancreatic (S13, 17, 18)		
	– Left gastric artery (S7)		
	– Common hepatic artery (S8)		
	– Celiac (S9)		
	– Hepatoduodenal ligament (S12)		
	– Superior mesenteric vessel (S14)		
	– Colic artery (S15)		
*fill in margins when applicable. If a margin is involved, indicate the distance and specify direct or indirect involvement	– Para-aortic (S16)		
	– Splenic hilum (S10)		
	– Superior splenic artery (S11)		
	LNR (positive nodes/total nodes):		
TNM classification (according to the current edition)**:**			
Comments:			

Appendix 5:New Proposed TNM Classification for AJCC Staging System for Pancreatic Adenocarcinoma (Eight Edition) [100]

Primary tumor (T)			
T1: Maximum tumor diameter ≤ 2 cm T2: Maximum tumor diameter > 2 ≤ 4 cm T3: Maximum tumor diameter > 4 cm T4: Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)			
Regional lymph nodes (N)			
N0: No regional lymph node metastasis N1: Metastasis in 1–3 regional lymph nodes N2: Metastasis in ≥4 regional lymph nodes			
Distant metastases (M)			
M0: No distant metastases M1: Distant metastases			
Stages			
Stage IA	T1	N0	M0
Stage IB	T2	N0	M0
Stage IIA	T3	N0	M0
Stage IIB	T1–T3	N1	M0
Stage III	Any T	Any N	M0
	T4	N2	M0
Stage IV	Any T	Any N	M1

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27 Preoperative Nutritional Status, Postoperative Nutritional Support, and Clinical Outcome Following Pancreatic Surgery

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27.1 Preoperative Nutritional Status

The high prevalence and negative effects of malnutrition for hospitalized patients are well known and have been studied intensively [1–10]. However, the definition of a malnourished status varies widely, and different modalities are used to define the status. For example, measurements like the body mass index (BMI), bioimpedance, radiological cross-sectional imaging, or laboratory values like serum albumin level can be used. Further, nutritional assessment scores were developed which consist of measurements and questions concerning weight progression, diet, and other risk factors for malnutrition. There are many different scores which are validated in different patient populations [11]. For a variety of surgical fields, lots of studies have been done to determine the prognostic value of malnutrition for postoperative complications. Most of these studies suggest that preoperative malnutrition is linked to a higher postoperative morbidity and mortality. A systematic review by Sun et al. [12] from 2015 found higher mortality and higher postoperative complication rates for abdominal surgery patients diagnosed as malnourished by Nutritional Risk Screening 2002 (NRS2002) [13]. Another systematic review by van Stijn et al. [14] published in 2013 identified weight loss and serum albumin as predictive for postoperative outcome in elderly general surgery patients. Currently there are no systematic reviews or meta-analyses and only a limited number of studies concerning preoperative nutritional assessment and postoperative outcome in patients undergoing pancreatic resection. These studies were published between 2005 and 2013 and had a retrospective design. In a study by Schnelldorfer et al. [15], 313 patients with pancreatic surgery for chronic pancreatitis were analyzed. Also included were drainage operations like lateral pancreaticojejunostomy. Subjective Global Assessment (SGA), Nutrition Risk Index (NRI), and the Instant Nutritional Assessment (INA) score [16] were used to assess malnutrition and showed an association with postoperative complications. One hundred thirty-two patients after distal pancreatectomy were evaluated by Sierzega et al. [17], and the NRI and INA were assessed. The collected data stretches over 10 years. An NRI of 100 or less showed an association with pancreatic fistulas with an odds ratio of 8.12 (95% CI, 1.06 to 22.30). Onodera's version of the prognostic nutrition index (PNI) [18] was investigated by Kanda et al. [19]. For this 268 patients undergoing different resections for pancreatic cancer over 20 years were analyzed. The results showed that a low PNI was associated

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with poor survival and also higher postoperative complications. Shinkawa et al. [20] analyzed NRI and NRS 2002. Sixty-four patients undergoing pancreaticoduodenectomy were included over 7 years. The risk for surgical site infections was independently associated with low NRI. Another study by La Torre et al. [21] investigated 143 patients over 8 years. The participants underwent surgery for pancreatic cancer, and SGA, NRI, and Malnutrition Universal Screening Tool (MUST) [22] were analyzed. MUST and NRI showed an association with overall morbidity. These studies were retrospective, spanned over long periods of time, and lack a prior definition of a primary endpoint. Thus, their findings should be put into question. To determine the clinical usefulness of nutritional assessment scores, a prospective clinical trial has been conducted at the University Hospital of Heidelberg by Probst et al. [23, 24]. Twelve nutritional assessment scores were prospectively assessed for their prognostic value in patients undergoing pancreatic surgery. A total of 279 patients were analyzed over 1 year. Contrary to the beforementioned retrospective studies, no association with postoperative morbidity and mortality could be found. Looking at these results, the value of preoperative nutritional assessment scores is strongly questioned. Especially the lack of prior definition of a primary endpoint as well as the long time period in previous studies might explain the different results. Also a retrospective design has a higher risk of detection and reporting bias. The study by Probst et al. showed no association even when using the comprehensive complication index (CCI) [25] as a measurement for complications. It should be mentioned that the original intent of nutritional assessment scores was not to predict surgical complications. Whether or not they have a relevant role in assessing a patient's postoperative risk after pancreatic resection and the usefulness in daily clinical practice stays questionable. Therefore, additional tools to assess a patient's preoperative nutritional status with regard to postoperative outcome should be tested. Applying the amount of body fat as a predictor of postoperative outcome represents one such alternative. Literature shows differing results on whether a high and/or low body fat amount is detrimental to postoperative outcome. Also under discussion is the influence of obesity and postoperative morbidity [26–29]. In contrast to the abovementioned publications, several studies showed a link between cachexia and worse postoperative outcome [30, 31]. They showed a significant amount of weight loss for patients with unresectable pancreatic cancer and a steady decline until death. A more precise tool than BMI or weight loss to determine nutritional-related risk after pancreatic resection could be the diagnosis of cachexia by preoperative computed tomographic or magnetic resonance imaging scans, as described by Pausch et al. [32]. The imaging allows differentiating between different forms of fat. The study by Pausch et al. made the distinction between abdominal wall fat, hip girdle fat, and intra-abdominal fat. The cross-sectional imaging of 408 patients who underwent pancreaticoduodenectomy at the University Hospital of Heidelberg was analyzed for the amount of abdominal wall fat, hip girdle fat, and intra-abdominal fat. The results showed that specifically patients with high amounts of abdominal wall fat had lower morbidity, lower short-term mortality, and improved long-term survival. Also low BMI was associated with higher short-term morbidity and higher complication rates. Another study by Amini et al. [33] defined cachexia by using preoperative cross-sectional imaging to measure total psoas volume. The results showed association of total psoas volume with postoperative complications, short-term mortality, and long-term survival after pancreatectomy for pancreatic adenocarcinoma. No association was found using total psoas area. However, a study by Peng et al. [34] found an association with postoperative outcome using total psoas area as defining sarcopenia. Similar research was done by Joglekar et al. [35] in a retrospective review of a pancreatectomy database. Sarcopenia was assessed by determining the Hounsfield unit average calculation of the psoas muscle using preoperative computer tomography images. This definition of sarcopenia was independently predicting major complications and length of stay. While it remains

unclear which specific way of measuring sarcopenia and cachexia using cross-sectional imaging is most suitable, the general method seems promising in assessing a patient's individual postoperative risk after pancreatic resection. The current state of knowledge seems to point toward measurements obtained via cross-sectional imaging as a more promising and more reliable tool in predicting postoperative outcome than nutritional assessment scores. However, more research needs to be done to find the most suitable and most convenient way of obtaining those measurements. A definition of malnutrition that yields relevant clinical results remains still unclear.

27.2 Postoperative Nutritional Support

To date there is no general acknowledged gold standard for postoperative nutritional support in pancreatic surgery and many guidelines exist. The possibilities for postoperative nutritional support can be divided into oral, enteral, and parenteral. Hereby, enteral nutritional support can be delivered via nasogastric tube, nasojejunal tube, or a needle-catheter jejunostomy. Parenteral nutritional support is usually given through central venous catheter with standardized 3-in-1 products. It is generally agreed that oral or enteral nutrition has beneficial effects compared to parenteral nutrition whenever possible [36]. However, existing guidelines for postoperative nutritional support after pancreatic surgery vary significantly. The Enhanced Recovery After Surgery Society (ERAS) [37] recommends a restriction-free oral diet starting at the first postoperative day and increase intake over 3–4 days after pancreaticoduodenectomy. Enteral tube feeding should be restricted to selected patients, and parenteral nutrition should not be the standard course of action. However, in an ERAS program, there are many constraints other than nutrition. The American Society for Parenteral and Enteral Nutrition (ASPEN) has an even more restrictive approach [38]. ASPEN suggests no nutritional support when sufficient oral intake can be resumed within 7–10 days. The German Society for Nutritional Medicine (DGEM) [36] also suggests an early oral diet according to individual tolerance. Nutritional support is advised for patients that are not able to reach a daily oral intake of more than 60–75% of the caloric requirement for more than 10 days. Enteral support is preferred, and parenteral support should only be applied if sufficient caloric intake cannot be achieved by enteral support alone. Furthermore, there are studies suggesting that combined postoperative enteral and parenteral nutrition is more beneficial for patients after pancreatic surgery. Nagata et al. [39] showed that combined parenteral and enteral nutrition was superior for patients than enteral nutrition alone after pancreatic surgery. Similarly, a study by Zhu et al. [40] demonstrated that combined parenteral and enteral nutrition was more advantageous than parenteral nutrition alone in patients undergoing pancreaticoduodenectomy. Similarly, a study by Probst et al. [41] found comparable results for a European patient cohort. In the absence of a gold standard, further trials are needed comparing the three possible ways of nutrition: oral vs. enteral vs. parenteral or even of their combinations. As long as there is insufficient evidence, treating physicians can rely on their personal experience and on patient-individual needs.

27.3 Clinical Pathway for Patients Undergoing Pancreatic Procedures at the University Hospital of Heidelberg

Preoperative the NRS 2002 [13] is assessed in every patient. However, there is no change of the clinical pathway as the evidence from our own institution does not suggest a relevance [23, 24]. Every patient receives a structured education on the postoperative procedure with advices on mobility, nutrition, and training after the operation [42].

At the end of the operation, no gastric tubes are left in place and no needle-catheter jejunostomies are made routinely. After 4–6 h in the recovery room, patients are transferred to the normal

ward. Patients with vascular reconstructions normally go to intermediate care station for one night. Patients after total pancreatectomy stay 3 days on the intermediate care station.

Directly after the operation, patients are allowed to drink clear liquids and if possible leave the bed for the first mobilization with assistance. All patients have physiotherapy once a day and sometimes additional physical treatments [43].

Beginning from the first postoperative day, a stepwise progression to a normal full oral diet is attempted. Additionally, all patients receive a proton pump inhibitor and pancreatic enzymes. Patients receive oral nutritional supplements in first order if oral food uptake is prolonged or parenteral nutrition in case of inability to eat or complications. Feeding tubes are not standardly placed and are only the treatment of choice in patients with an anticipated long-term ICU stay. There is no standard nutritional counseling for patients undergoing pancreatic surgery except for patients with total pancreatectomy. The postoperative education on change in nutritional physiology is granted by the physicians.

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Pancreas-Sparing Duodenectomy: How I Do It

28

Monica M. Dua, Lavina Malhotra, and Brendan C. Visser

28.1 Introduction

It is well accepted that the standard operation for malignant duodenal neoplasms is pancreaticoduodenectomy (PD). Benign (or premalignant) duodenal tumors may be resected with a spectrum of techniques: endoscopic, local resection, duodenal sleeve (with preservation of ampulla), PPTD, and PD (in order from least to most tissue resected). PD is the most commonly performed operation for duodenal tumors and is thus the operation with which many surgeons are most comfortable. While improvements in surgical technique and perioperative management have decreased the overall operative morbidity associated with PD, it still suffers the inherent complications related to resection of the pancreas and the pancreatojejunostomy. Patients with duodenal neoplasms have a soft pancreatic parenchyma and thus a higher risk of pancreatic fistula formation after PD. In cases where preservation of the ampulla is not feasible, PPTD is sometimes an alternative to formal PD.

The basic principles of PPTD are to remove the duodenal mucosa in its entirety, maintain normal outflow pancreatic and biliary drainage, and preserve foregut anatomy. Chung and colleagues first reported PPTD in 1995 on five patients that underwent total duodenectomy for familial adenomatous polyposis (FAP) syndrome [1]. These patients required excision of the duodenum for complete clearance of polyps; the head of the pancreas was completely preserved, and reconstruction was accomplished by advancing the jejunum toward the pylorus to create an end-to-end anastomosis of the jejunum to the duodenal cuff just past the pylorus. Implantation of the biliary and pancreatic ducts was placed into the neoduodenum in a location that corresponded to the prior native papilla. The presence of a direct gastrojejunal anastomosis allowed for continued long-term endoscopic surveillance. FAP remains the most common indication for PPTD, though essentially any other neoplastic process confined to the duodenal mucosa without potential for spread along the periduodenal lymphatics can be resected via PPTD. Sporadic large ampullary adenomas or other solitary, broad-based adenomas of the duodenum are also defined indications for PPTD [2–12]. Certainly, more uncommon indications that have been reported as single case studies or case series include PPTD for trauma resulting in duodenal necrosis [2], neuroendocrine tumor [4, 12], stromal tumor [9], amyloidosis [11], lymphoma [8], liposarcoma [3], and giant hamartoma [5]. Advantages of this procedure over PD include preservation of the entire pancreas with inherent decreased risk of

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endocrine or exocrine insufficiency, reduced number of anastomoses, and increased ease of endoscopic surveillance of the neoduodenum if required.

28.2 Relevant Anatomy

The duodenum proximal to the ampulla of Vater is intimately adherent to the pancreatic head as the pancreatic parenchyma grows into the muscular and subserosal layers of the duodenum. A dissection plane surrounding the ampulla is difficult to develop in this region, and separation is achieved by intramural dissection of the duodenum leaving the outer muscular layers of the duodenal wall attached to the pancreatic head. In contrast, the plane of dissection between the pancreas and the infra-ampullary duodenum is much easier to define, yet traversed by a number of small vessels along the curve of the pancreatic head.

The arterial system of both the duodenum and head of the pancreas consist of an anterior and posterior group of arcades that include the superior and inferior pancreaticoduodenal arteries, respectively. Both superior arteries arise from the gastroduodenal arteries, while the inferior branches arise ultimately from the superior mesenteric artery via the inferior pancreaticoduodenal artery. The pattern of venous drainage may vary, but all small tributaries eventually drain into the superior mesenteric or portal veins. Both the arterial supply and the venous drainage of the duodenum consist of terminal vessels arising from vessels more centrally located within or around the pancreatic head. Despite the common blood supply of the duodenum and pancreatic head, resection of the former does not devascularize the later [13].

28.3 Surgical Technique

Surgical exploration is typically performed through a midline incision. The initial step is to rule out the presence of metastatic or invasive duodenal disease which would be a contradiction to PPTD. A wide Kocher maneuver across the midline to the level of the aorta greatly allows for manual palpation of the second portion of the duodenum, especially around the ampulla. A cholecystectomy is performed to open the cystic duct and cannulate this with a cholangiogram catheter or Fogarty catheter (both have a balloon tip that can be inflated and palpated) to facilitate identification of the ampulla in the setting of large ampullary polyps or adenomas (Fig. 28.1). A point approximately 10 cm distal to the ligament of Treitz is chosen for division of the bowel in the infracolic compartment. The jejunum is divided with GIA stapler, and the proximal end is used as a handle to start freeing the distal duodenum. The short mesenteric vessels are divided and tied or sealed at the root of the mesentery to the level of the uncinate (much like as is done for PD). The transected bowel is then flipped through the root of the mesentery and posterior to the superior mesenteric vessels to end up on the patient's right side. Meticulous dissection continues along the interface of the pancreas and the distal duodenum taking all small vessels in continuity either with a vessel seal, clips, or ties. Once the ampulla is reached from the distal dissection, the duodenum is divided just past the pylorus with another load of the GIA stapler. Proximal transection of the duodenum allows for appropriate traction of the duodenum laterally to allow the dissection to be continued medially along the first and second parts of the duodenum.

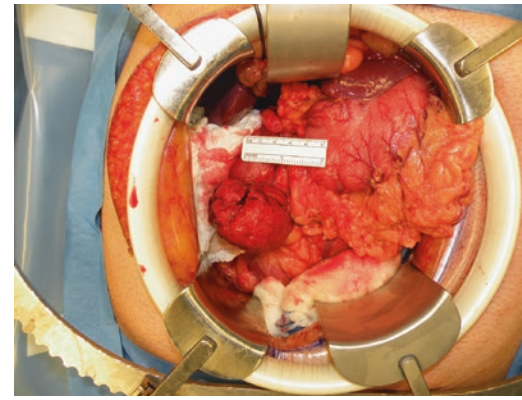

Fig. 28.1 An example of a near-occlusive large polypoid mass with circumferential extension from the second portion of the duodenum

At the ampulla, the bile duct and pancreatic duct are transected sharply where they enter the

duodenal wall. This is facilitated by holding the freed duodenum on tension to the patient's right. The ampullary margin is sent for frozen section, and the two ducts are spatulated and sutured together to provide a common channel for a single anastomosis (Fig. 28.2). The distal end of the jejunum is brought through the bare area of the transverse colon mesentery to the right of the middle colic vessels, and the antimesenteric side of the bowel is aligned with the common ductal channel to create a two-layer duct-to-mucosa anastomosis (Fig. 28.3) as in a modified Blumgart pancreaticojejunostomy [14]. Caution is required such that these sutures don't catch the bile duct; the catheter placed into the bile duct and use of intraoperative ultrasound can assist in this. Three transpancreatic silk (typically 2-0 silk on an MH needle due to the thickness of the head) U-sutures are placed about 1 cm from the edge of the pancreas and go through the parenchyma from anterior to posterior. The same suture is then used to take a horizontal seromuscular bite of the jejunum prior to complete the posterior layer prior to coming through the pancreas again from posterior to anterior. Three of these sutures are placed with the middle U-stich spanning the common channel. These sutures serve as a posterior row (like a Lembert stitch but without the risk of pulling through the capsule of the pancreas) and are tied with the needles left intact for creation of the anterior outer row after the duct-to-mucosa anastomosis. After creating a small enterotomy in the jejunum, the common channel and enterotomy are anastomosed together with interrupted synthetic absorbable monofilament sutures made of polydioxanone (PDS). Finally, the outer anterior horizontal mattress sutures are placed on the jejunum using the needle attached to the previously placed U-sutures and tied individually on the anterior surface of the pancreas (Fig. 28.4).

Gastrointestinal continuity is established by bringing the jejunum distal to this new anastomosis anterior to the transverse colon for a duodenojejunostomy much like is performed for a pyloric preserving PD. A closed suction Jackson-Pratt drain is placed in the surgical field in the region of the bili-

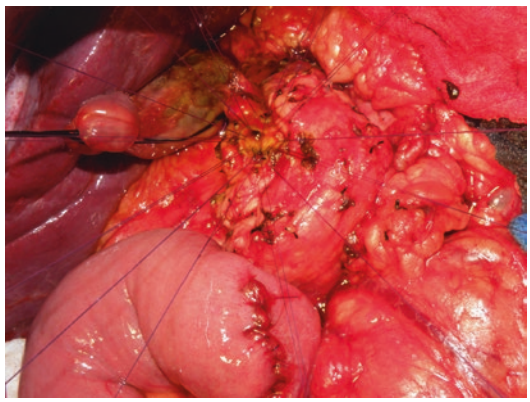

Fig. 28.2 The common bile duct and pancreatic duct channels were slightly spatulated and sutured together to provide a common channel for a single anastomosis

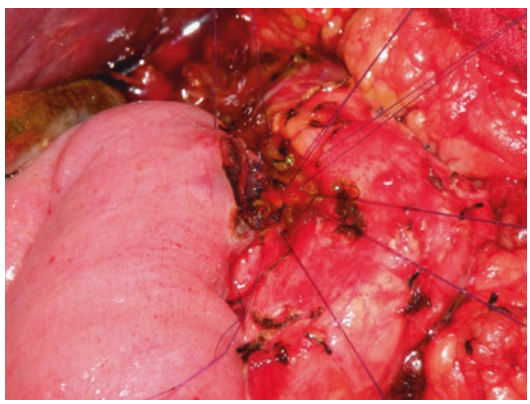

Fig. 28.3 The antimesenteric side of the jejunum is aligned with the common ductal channel to create a duct-to-mucosa anastomosis

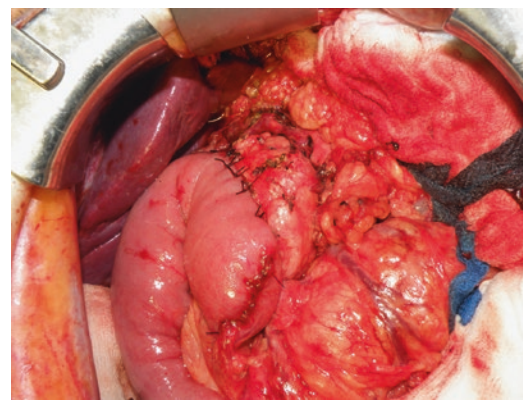

Fig. 28.4 The completed two-layer anastomosis is seen with the outer horizontal mattress silk sutures of the jejunum brought to the anterior surface of the pancreas

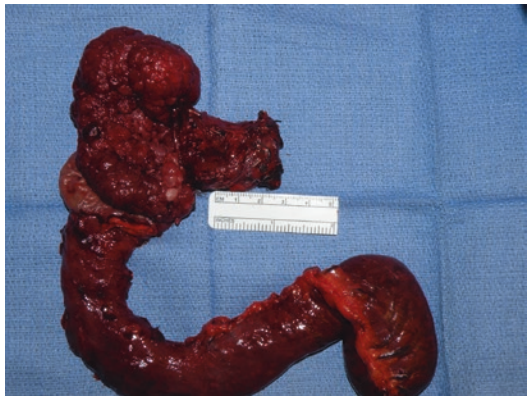

Fig. 28.5 The "C"-shaped duodenal specimen is shown with the large polypoid mass visible superiorly. The position of the obliquely oriented pancreas, which was not resected, can be appreciated in the specimen

ary and pancreatic anastomosis. An example of a "C"-shaped duodenal specimen is seen in Fig. 28.5.

28.4 Postoperative Management

Standard postoperative length of stay (LOS) is typically 7–10 days. A liquid oral diet is started around day 3 after surgery and advanced to a regular diet as tolerated. Routine nasogastric tube drainage is not required but only inserted for symptoms consistent with delayed gastric emptying. The JP drain by the anastomosis is removed prior to discharge if the output looks benign and the drain amylase level is low; it is left in place if there is suspicion for a leak. Even in those cases, if the patient is clinically well and meeting all other criteria for discharge, they may be sent home with the drain and managed as an outpatient. The primary early postoperative complications include anastomotic fistula, delayed gastric emptying, pancreatitis, and wound infection.

28.5 Reported Variations in Technique

The techniques of ampullary reconstruction have varied in literature. Historically, Chung et al. described reconstruction following resection by advancing the jejunum toward the pylorus, to perform an end-to-end anastomosis with the jejunum and proximal cuff of duodenum to create a "neoduodenum." Implantation of the bile and pancreatic ducts was established separately in a location corresponding to the native papilla of the neoduodenum. This was performed by a "through-and-through" intrajejunal approach, through an access enterotomy opposite the proposed site for reimplantation [1].

Tsiotos and Sarr significantly modified this procedure and used an extrajejunal approach for a single ampullojejunostomy after the pylorojejunostomy was created. This is facilitated by suturing to the common channel or by suturing the two ducts together so that a single anastomosis around both ducts can be performed. Once the optimal site on the jejunal wall facing the ampulla is selected, a one-layer duct-to-mucosa anastomosis is created using interrupted absorbable monofilament sutures (PDS). The posterior layer takes full-thickness bites of the posterior ampullary wall (inside-out) and full-thickness bites of the posterior duodenal wall (outside-in). All stitches are aligned and placed prior to being tied leaving the knots on the inside of the anastomosis. The anterior layer is performed in a similar fashion, with full-thickness bites through the anterior ampullary wall (outside-in) and anterior duodenal wall (inside-out), and the knots are tied on the outside of the anastomosis to complete the anastomosis in the fashion most surgeons use for a traditional hepaticojejunostomy [13].

Reconstruction techniques similar to a Whipple reconstruction have been reported in which an end-to-side pancreaticojejunostomy is performed to the head of the gland followed by end-to-side duodenojejunostomy or gastrojejunostomy [7]. Reconstruction with end-to-side invagination pancreaticojejunostomy without duct-to-mucosa suturing of ampulla has also been reported. In this technique, the jejunum is fixed to the intact head of the pancreas anteriorly and posteriorly by interrupted nonabsorbable sutures beyond the ampulla [2].

Pancreatic divisum is the most common congenital variant of pancreatic duct development and occurs in up to 18% of individuals [15]. In these cases, the dorsal pancreatic duct drains separately form the ventral duct. Thus, for a PPTD,

two separate duct-to-mucosa anastomoses or the invagination technique is required to prevent obstructive pancreatitis [10].

A minimally invasive approach to PPTD was first reported by Benetatos and colleagues [16]. This was followed by two other cases reported by Stauffer et al. [17] from a group that has vast experience with laparoscopic PD. Both employed similar dissection techniques using a laparoscopic ultrasonic-activated scalpel to maintain a clean and hemostatic dissection plane for separation of the duodenal-pancreatic head complex. Cholecystectomy with placement of a transcystic catheter through the ampulla of Vater was performed to facilitate identification of the major papilla. The operating times of the laparoscopic approach were very long in both reports (between 450 and 593 min) but with minimal blood loss and low morbidity.

28.6 Discussion

The surgical management of duodenal neoplasia remains complex. Endoscopic resection, local excision (including ampullectomy), sleeve resection of the duodenum (with preservation of the ampulla), pancreas-preserving total duodenectomy, and PD are all employed. Advanced endoscopic techniques may have a role for small, localized duodenal tumors in patients that would otherwise not tolerate a resection [18]. Duodenal polyps that are large in size, located close to the ampulla, or associated with a polyposis syndrome require complete removal of the duodenum along with the periampullary region via PPTD or PD for definitive management and to minimize recurrence [19]. While reports on PPTD have continued to emerge, the surgical community has been slow to adopt this procedure as evidenced by the paucity of data on long-term outcomes. Moreover, the terminology of pancreas-sparing duodenectomy (PSD) and pancreas-preserving total duodenectomy (PPTD) has varied in literature making the outcomes difficult to compare. PPTD is principally performed for ampullary lesions and diffuse lesions of the duodenum. Pancreas-sparing partial duodenectomy (PSPD) has been described for supra-ampullary and infra-ampullary lesions not amenable to endoscopic resection or wide local excision. In PSD, only partial dissection of the duodenal-pancreatic head complex is required at either the proximal or distal head of the pancreas-duodenum junction and advanced pancreaticobiliary reconstruction is unnecessary. PPTD is not an oncologically appropriate operation for invasive duodenal lesions, and it is crucial not to compromise safe resection margins for organ preservation. The combination of preoperative endoscopic ultrasound or magnetic resonance imaging and intraoperative pathological analysis can often reliably exclude this possibility; however it is prudent to counsel patients prior to surgery that the extent of disease may require conversion to formal PD.

A recent literature review found 128 unique cases of PPTD with overall mortality and morbidity rates of 2.3% and 46.4%, respectively [17]. The most common complications were pancreaticobiliary leak (16%) and delayed gastric emptying (12%), with mean hospital LOS being 17 days. Three studies compared results of PPTD to those from similar patients undergoing PD to determine any difference in outcomes. The first study from the Netherlands compared 26 patients with FAP who underwent PPTD to 77 patients with ampullary adenocarcinomas who underwent PD [20]. They found longer operative times for PPTD but similar complications, LOS, and mortality. A high rate of jejunal limb ulceration (19%) was seen in the PPTD group compared to no cases in PD which led them to change their practice to a Roux-en-Y reconstruction for gastrointestinal continuity. In the follow-up period, 12% of patients in the PD group developed diabetes compared to none in the PPTD group. Overall, they did not find any clear advantage of PPTD over conventional PD. The second group from Germany compared the results of 16 patients undergoing PPTD to 16 matched patients undergoing pylorus-preserving PD and found comparable morbidity, mortality, and LOS, but lower operative blood loss for PPTD patients [4]. Long-term follow-up demonstrated 75% of the PD group to require oral pancreatic enzyme supplementation compared to none in the PPTD group. Quality-of-life analysis between the two groups was also performed and showed no significant differences. The third study from Cleveland clinic [7] compared 21 patients undergoing PPTD

to 238 patients undergoing PD for various indications. Typical PPTD reconstruction in this study was an end-to-side pancreaticojejunostomy (pancreatic and biliary orifices reconstructed together via one enterotomy) with an advanced jejunal limb. They found similar LOS, complication rates, and mortality and, however, a higher pancreatic leak rate among patients undergoing PPTD (19% versus 9%). Despite these observations, no prospective data is available comparing PPTD to PD.

Conclusion

PPTD is a technically challenging procedure that is feasible in highly selected patients in whom malignant disease has been excluded. It is best suited for patients with noninvasive adenomatous disease of the duodenum with no pancreatic involvement, and postsurgical endoscopic surveillance is possible directly through the gastrojejunal anastomosis. In experienced centers, PPTD can be performed with comparable morbidity to PD and may provide some long-term benefits such as decreased endocrine and exocrine insufficiency. Although still a relatively novel technique, PPTD serves as an additional surgical strategy for the resection of benign duodenal lesions.

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