



Laparoscopic Pancreaticoduodenectomy

Le Quan Anh Tuan and Pham Minh Hai

Introduction

Evolution and difficulties of Laparoscopic pancreaticoduodenectomy.

Pancreaticoduodenectomy (PD), understood as radical pancreaticoduodenal resection at present, was popularized by Allen O. Whipple and colleagues [1]. At that stage, this procedure is associated with a high rate of morbidity and mortality. With natural evolution, developments in equipment and technically surgical skill had been appearing. Gagner and Pomp [2] successfully performed laparoscopic pancreaticoduodenectomy (LPD) in 1994. The procedure's popularization was still low, especially over the next decade. This is due to high rate of postoperative complications and technical difficulties. Pancreatic head and duodenum are located deeply in retroperitoneal space and are close to major vascular structures. These result in difficulties in performing LPD. Moreover, life-threatening

complications can happen if these major vascular structures are injured.

In recent years, outcome of LPD has been significantly improved owing to developments of surgical technique, medicine and equipment, and energy devices, for example. LPD has become more common all over the world. However, this is still a challenging procedure.

LPD consists typically of standard LPD, LPD with arterial first approach, and LDP with superior mesenteric-portal vein resection. This chapter's purpose is to describe technically the former.

Indications

LPD is generally indicated for below conditions:

1. Resectable and borderline resectable periampullary cancers
2. Targeting of malignant pancreatic head neoplasms (IPMN)
3. Chronic pancreatitis with inflammatory mass in pancreatic head
4. Benign periampullary neoplasms not amenable to local resection

Patient Selection

Theoretically, most indicated PD is able to perform LPD. Because of certain limitations as proceeding LPD such as higher abdominal pressure

L. Q. A. Tuan (✉)

Department of Hepatobiliary and Pancreatic Surgery, University Medical Center, Minimally Invasive Surgical Training Center, Ho Chi Minh City, Vietnam

Department of General Surgery, University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam
e-mail: tuan.lqa@umc.edu.vn

P. M. Hai

Department of Hepatobiliary and Pancreatic Surgery, University Medical Center, Ho Chi Minh city, Vietnam

which can cause consequences for respiratory and cardiac systems. Because LPD operating time is long, patients with severe respiratory and cardiac disease should be eliminated. Apart from this, vascular resection and reconstruction require a high level of laparoscopic surgical skills, longer time and they can cause more blood loss as well. Although authors can do LPD with borderline resectable tumors belong to periampullary pathologies, other authors have recommended that borderline resectable tumors are only performed at a few specialized centers; indication for LPD in cancer patients should be limited at resectable stage.

Procedure

Generally, there are two main procedures in classification. One is classic PD called Kausch-Whipple. Another one is pyloric preservation PD (PPPD) which was described by Longmire and Traverso. Both can be done by a minimally invasive approach such as laparoscopic surgery.

Operating Room Setup, Patient Positioning, and Surgical Team

Appropriate operating room may require a flexible table, cautery system, and energy system. Ideally, there are two monitors located at the head of the bed over both shoulders' side. One is for the surgeon and scrub nurse and another is for assistants. When lack of facility, given just one monitor, the placement should be on the left side of the patient.

Patient is placed in supine with slight head up. With head up, we can have better view resulting from gravity retraction. Patient's legs should be split to make space for cameraman. Arms are tucked to create free spaces for surgeon, assistants, and scrub nurse's activities.

The main surgeon and scrub nurse are positioned on the patient's right side. The first assistant's (cameraman) position is between patient's legs and second assistant stands on the left side. The back table is set up on the right side of patient, above the scrub nurse. The personnel is described as in Fig. 1.

Technique

There are two main phases included in laparoscopic pancreaticoduodenectomy. They are resection and reconstruction.

Trocar Placement

First trocar is 12 mm in size which is placed at umbilicus' left side by Hasson technique.

One 12 mm trocar and three 5 mm trocars are placed as in Fig. 2.

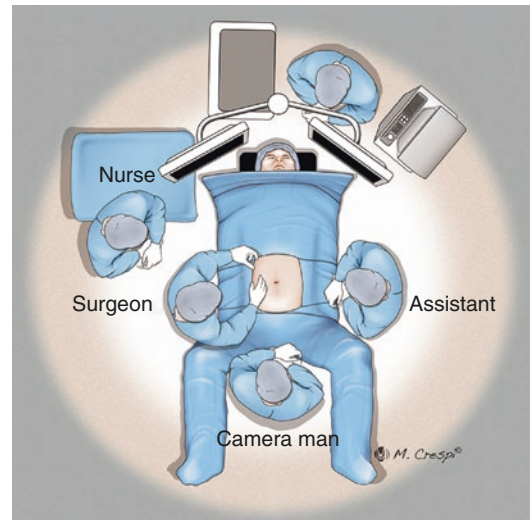


Fig. 1 OT setup

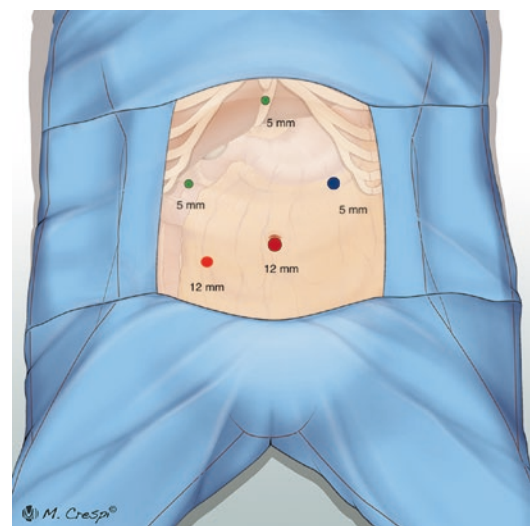


Fig. 2 Port placement

Inspection

Staging is very important in case of malignant or suspected malignant lesions. This is a mandatory step. Abdominal inspection is performed to assess liver, peritoneal, and mesenteric metastases. Beside this, we can assess resectability of tumor.

Dissection Phase

There are different approaches for LPD. We usually use clockwise approach for dissection phase. However, all patients were not applied the same kind of approach. It depended on proper situation. In case of a tumor located in uncinate process, we used superior mesenteric artery first approach. Clockwise approach includes below steps. Before these steps are described in detail, it is necessary to consider levels of lymphadenectomy in LPD. There are three levels of harvesting lymph nodes, but we only focus on standard lymphadenectomy which is recommended to perform routinely at present.

A consensus statement by the International Study Group on Pancreatic Surgery (ISGPS) was published in 2014 [3]. “After evaluating all the available literature and the expert opinions during the consensus meeting, a clear definition of a standard lymphadenectomy was reached: A standard lymphadenectomy should include Ln stations 5, 6, 8a, 12b1, 12b2, 12c, 13a, 13b, 14a right lateral side, 14b right lateral side, 17a, and 17b” (Fig. 3).

Infra-pancreatic Superior Mesenteric Vein Exposure

After abdomen is carefully explored and signs of advanced stage are not found, the lesser sac is entered by dividing gastrocolic ligament below the level of gastroepiploic vessels. Gastrocolic ligament should be divided from the left side to the duodenum to create enough space for working around head and body of pancreas. During this, transverse mesocolic vessels can be injured because of adhesion, especially at the site of pancreatic head. Avoiding these consequences, tips are following gastroepiploic vessels and duode-

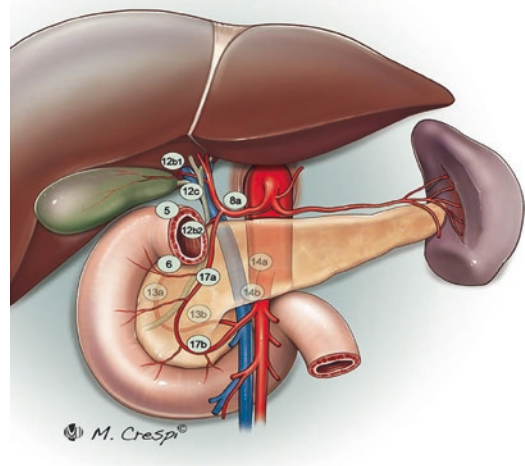


Fig. 3 Standard lymphadenectomy during PD

num. Moreover, meticulous dissecting is required. Greater omentum can become partly ischemic after dividing gastrocolic ligament but we do not need to resect it mostly.

Superior mesenteric vein (SMV) is dissected at inferior pancreatic border (Fig. 4). Right gastroepiploic and middle colic vein are important landmarks. SMV is covered by a thin layer called adventitial tissue and loose thin connective tissue outer. Dissector forceps can be useful to dissect and enter the loose thin connective tissue around SMV to expose SMV. Middle colic vein can drain separately or join with gastroepiploic vein to SMV. We prefer to leave middle colic vein unless it impedes such as in SMA first approach or some variations. Gastroepiploic vein must be ligated at the site draining to SMV as it drains separately. When gastroepiploic and superior right colic vein form gastrocolic trunk of Henle, the latter should be preserved.

SMV and portal vein (PV) exposures are slowly developed upward till superior border of pancreas. This work is recommended under viewing. Expanding our dissection to the left of SMV facilitates this work. During expanding dissection, we need to consider vessels nearby SMV.

Extended Kocher Maneuver

Right border of SMV is used to follow to push transverse mesocolon away from pancreatic head. Beside gastroepiploic and anterior pancreatico-

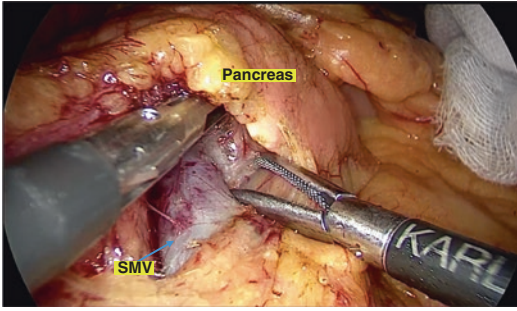


Fig. 4 Infra-pancreatic superior mesenteric vein (SMV) exposure

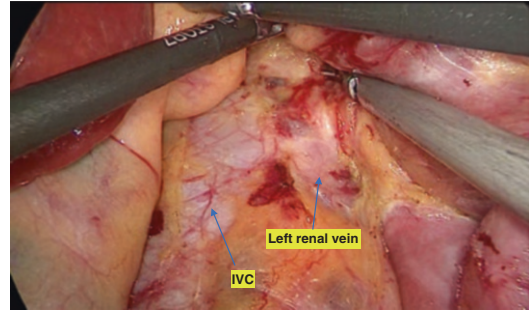


Fig. 6 Kocher maneuver

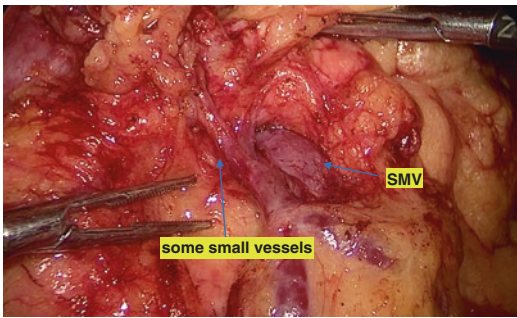


Fig. 5 Some small branches across dissecting plane

duodenal vein, there are some small vessels across this plane (Fig. 5). They usually cause bleeding during dissecting this plane that is difficult to control. Sharp dissection with energy devices shows effectively. Then duodenum part three and part four are separated from transverse mesocolon.

In laparoscopic surgery, it is easier for Kocher maneuver if this is dissected cephalad. Extended Kocher maneuver is completed when not only duodenum, pancreatic head, and uncinate are separated from retroperitoneum but inferior vena cava (IVC), left renal vein, and SMA are also exposed (Fig. 6).

Duodenal or Antral Transection

Pylorus preserving pancreaticoduodenectomy has been usually performed if signs of duodenal invasion have not appeared. It was preferred although delayed gastric empty was reported higher than classic PD.

It is similar to open surgery duodenum transected below pylorus 2–3 cm in LPPPD. Lymph

node group 5 and 6 will be left to remove en bloc with pancreatic head. For laparoscopic classic PD, antrectomy is performed at the level of third or fourth transverse vein on lesser curvature and at the confluence of the gastroepiploic veins on greater curvature. We use stapler for this step.

Upper Border of Pancreatic Neck Dissection and Gastroduodenal Artery Ligation

In laparoscopic PD, duodenal or antral transection (step 3) should be done prior this step and next step (dissection of porta hepatis) like outline in this chapter. In the condition of open PD, step 3 is usually performed when ability of radical tumor resection is ensured. This means step 3 has to follow step 4, 5, and 6. The explanation is because in LPD all laparoscopic instruments go upward from the ports and direction of dissection is in cephalad as well. Thus, surgical viewing becomes better after completing step 3 (Fig. 7). One more important tip to have good exposure to this area is liver retractor. We prefer liver retractor as in Fig. 8.

Anatomical variations may lead to inadvertent missing. Most of the major variations such as hepatic or gastroduodenal arterial anomalies, SMA, and bile duct variations are well identified on CT scan preoperatively. Among them, we need to care with accessory or replaced HA due to easily advertently missing (Fig. 9).

We usually started at upper border of pancreatic neck by incising the fascia and taking away large lymph nodes along common hepatic artery (CHA), lymph node group 8a. As a result, CHA was exposed. Follow CHA to extend lymphade-

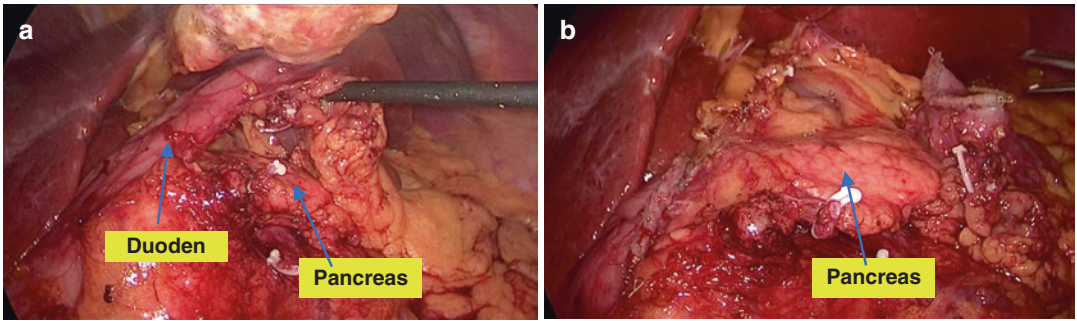


Fig. 7 Difference of surgical view between before (a) and after (b) duodenal or antral transection in laparoscopic PD

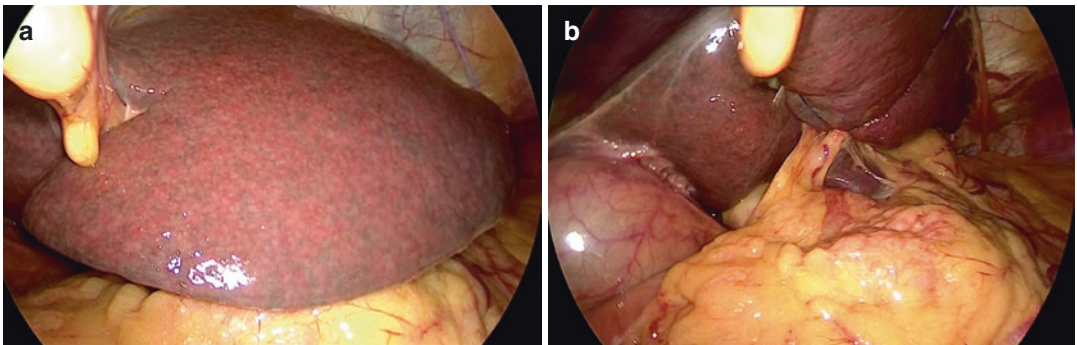


Fig. 8 Liver retractor: before (a) and after (b)

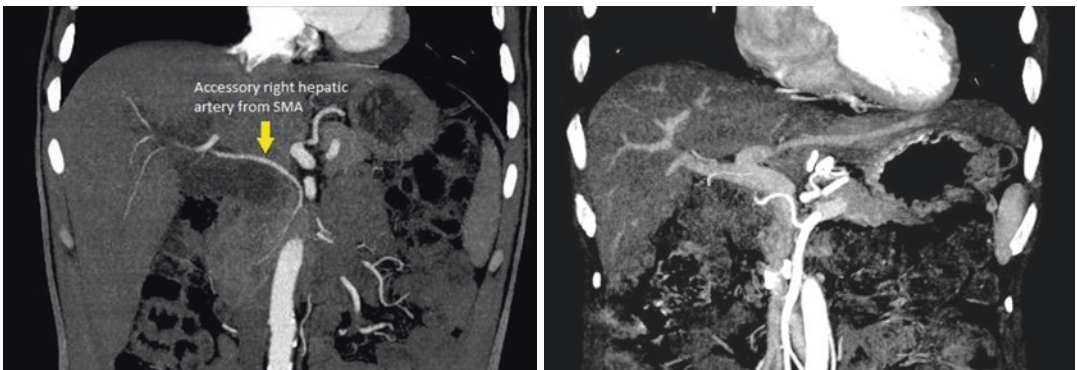


Fig. 9 Accessory or replaced right HA

nectomy bilaterally. According to standard lymphadenectomy, lymph node dissection is extended to left gastric artery (LGA) at level of Celiac trunk in left direction. It is taken into consideration of preserving left gastric vein which drains to PV or PV–SMV junction or splenic vein. Continuing dissection toward right side, right gastric artery and GDA are exposed clearly and ligated. For GDA

ligation, we prefer to tie it with suture 2.0 as Vicryl or silk. Supra-duodenal branches should be divided to make a free space enough. Checking by bulldog before dividing GDA is necessary as in Fig. 10.

Dissection of Porta Hepatis

Dissection of porta hepatis is also one part of lymphadenectomy. First of this step is separation

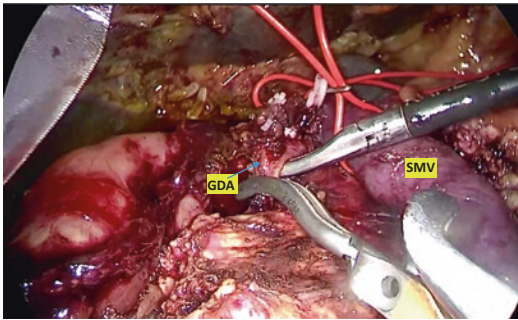


Fig. 10 Checking by using Bulldog before ligating GDA

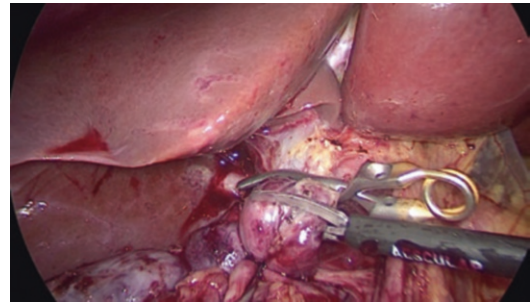


Fig. 11 Clamping bile duct before dividing

of fascia covering anterior porta hepatis to remove all fat and fascia around common hepatic duct (CHD), common bile duct (CBD), and cystic duct en bloc with CBD and gallbladder. These consist of lymph node groups namely 12b1, 12b2, and 12c belonging to the Japanese classification. After CBD, gallbladder and around tissue are taken down, PV is exposed. Despite not being included in standard lymphadenectomy definition, all fat and fascia surrounding HA and PV (group 12a and 12p) are practically taken away. These will be removed en bloc with lymph node group 8a, pancreatic head, bile duct, and duodenum at last dissecting step below. Although anatomical variations have been checked preoperatively, replaced or accessory right hepatic artery running right lateroposterior to CBD and CHD should be found during dissection of tissue surrounding PV and HA. Proximal stump of bile duct should be temporarily clamped by a bulldog and distal stump of bile duct should be ligation as well to prevent bile leakage as in Fig. 11. Biliary culture is recommended.

Pancreatic Neck Transection, Uncinate Dissection, and SMV, SMA Separation

Pancreatic neck transection is irreversible step on PD. Hence, it is usually completed when we believe that ability of doing PD is certain. This means SMA is able to separate from the tumor. We can check this by preoperative abdominal CT scan in most cases. However, we will get difficulty in suspicious cases. Actually, sureness is only achieved when we do arterial first approach. Arterial first approach is necessary in case of sus-

picious invasive SMA. This usually happens with tumors located in uncinate process. This is the reason why authors advise to perform uncinate dissection before pancreatic neck dissection, especially for open surgery.

For uncinate dissection, Treitz ligament is divided to give advantages for retractor duodenum and small bowel right laterally. Small venous branches draining to first jejunal vein and inferior pancreaticoduodenal vein are ligation to free SMV. Clip and energetic devices such as thunder beat and harmonic scalpel show effectively. First jejunal vein which curves postero-medially from the right side of SMV to course then posterior to SMA is usually protected. With our experience, if the ability of resection is almost certain, uncinate dissection will become easier and more advantageous after pancreatic neck transection.

Regarding pancreatic neck transection, tunnel under pancreatic neck which is created partly at the above steps is continued to complete. One tape is passed through this tunnel to lift pancreatic neck as transecting. After that pancreatic neck is transected at the level of SMV—PV.

Continue ligation of small branches draining to SMV and PV, usually from 3–5, to free completely SMV and PV as well. Then, SMV and PV are retracted left laterally to facilitate exposure of SMA wherein inferior pancreatic duodenal and first jejunal arteries are found. Inferior pancreatic duodenal artery (IPDA) may be divided in this step (Fig. 12) while first jejunal artery is usually protected. However, lymph nodes at origin of the latter should be harvested (Fig. 13) showing SMV and SMA separation.

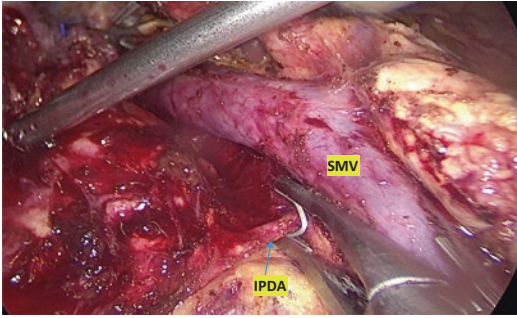


Fig. 12 Ligation of IPDA

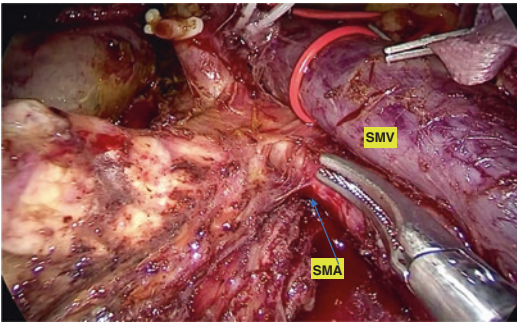


Fig. 13 SMV, SMA separation

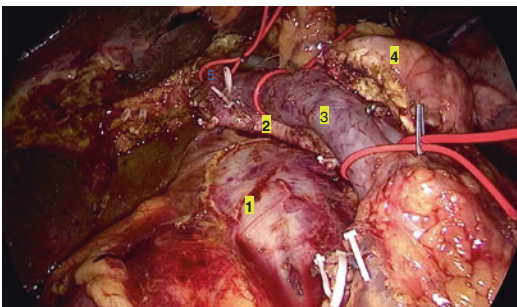


Fig. 14 After specimen removal in case of replaced RHA delivering from SMA (1: IV, 2: SMA, 3: SMV, 4: pancreas, 5: replaced RHA)

Jejunal Transection and Specimen Removal

Jejunum is transected by a stapler about 10 cm from Treitz flexure. Mesentery of proximal small bowel and connective tissue at the right side of SMA including lymph node group 14a and 14b are divided from SMA en bloc. Thus, the dissection phase is completed (Fig. 14).

Reconstruction Phase

Pancreatoenteric Reconstruction

At present, there is a range of procedures to do pancreatoenteric anastomosis. They are typically grouped into three main types with similar characteristics each. They are pancreaticogastrostomy, duct to mucosa pancreatojejunostomy (with or without parenchymal sutures), and invaginating pancreatojejunostomy. Although they are studied extensively, no kind is offered clearly superior to others in terms of improved outcomes [4–13]. Our team is in favor of end-to-side, two layers duct to mucosa pancreatojejunostomy.

Firstly, residual stump of jejunum is passed through transverse mesocolon where Treitz's ligament is divided. It is brought and placed close to pancreatic remnant. The latter is dissected to free approximately 1 cm from cut edge. Slowly absorbable suture monofilaments or bar sutures with 4.0 size are used for posterior parenchymal layer with continuous stitches. Next step is to open a hole at intestinal wall. Diameter of hole is equal to that of pancreatic duct. Then duct to mucosa suture is performed by interrupted stitches with absorbable suture (such as PDS) 4.0 or 5.0. We usually use an internal stent (Fig. 15) to ensure duct to mucosa pancreatojejunostomy working better and to prevent obstruction as well. Suturing to close anterior pancreatic parenchyma and jejunum is similar to posterior layer. Suction and irrigation around pancreatic anastomosis are performed carefully. This will be repeated once after completing hepaticojejunostomy to prepare for collecting fluid around pancreatic anastomosis. This fluid will be exam-

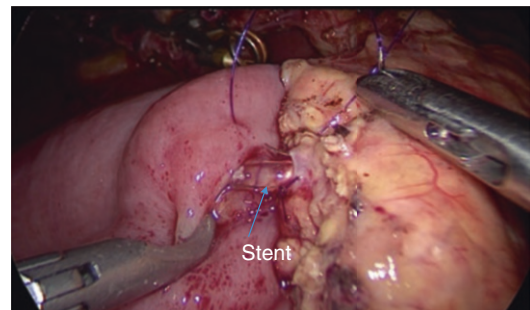


Fig. 15 Pancreatojejunostomy with internal stent



Fig. 16 Completed pancreaticojejunostomy (a) and hepaticojejunostomy (b)

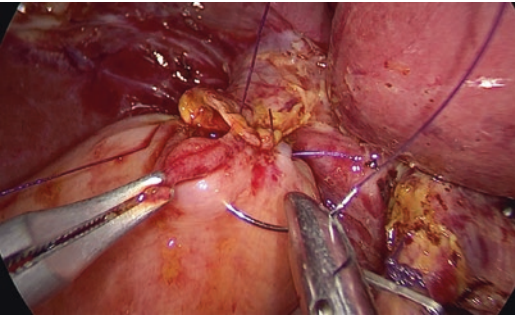


Fig. 17 End-to-side hepaticojejunostomy

ined for amylase concentration which can be used to evaluate the risk of postoperative pancreatic fistula. In the condition of unfound pancreatic duct due to very small size, we do pancreatojejunostomy like above procedure with only parenchymal layer and bigger opening on jejunum.

Hepaticojejunal Reconstruction

All three anastomoses including pancreatojejunostomy, hepaticojejunostomy, and enteroenteric anastomosis are performed with the same loop of jejunum (Fig. 17). End-to-side anastomosis is used for hepaticojejunostomy (Fig. 16). We prefer 4.0 or 5.0 absorbable sutures for this step. Continuous suture is used for both posterior and anterior half of hepatic duct's circumference if its diameter is upward of 5 mm. In contrast, if hepatic duct is less than 5 mm, we usually use interrupted suture. Important attention must be paid in this step to find the distance between pancreatic and hepatic duct anastomoses. This is not too long to avoid obstruction due to bending. Biliary stent is unnecessary. Authors routinely

stay jejunal limb to hilar plate to minimize tension of hepaticojejunostomy.

Enteroenteric Reconstruction

Duodenojejunostomy or gastrojejunostomy is technically easier than pancreatic and hepatic duct anastomoses. Hence, it is not difficult to do the former with totally laparoscopic surgery. However, expanding the incision of trocar to remove specimen (Fig. 18) is inevitable. Authors do it extracorporeally to save time instead.

Finally, checking for coagulation, bile leakage, gauze removal, and fluid clearance are completed. Drains are placed anterior pancreatic anastomosis and hepaticojejunostomy as well. Abdominal fascia defects and skin incisions are closed.

Complications and Management

Laparoscopic pancreaticoduodenectomy is a major surgery. When doing LPD, there will be common morbidities like other major surgery but the complication rate of LPD is higher. Moreover, there are complications only related to pancreatic resection. These can affect severely patients' health and lead to mortality [14]. Typically, there are three proper complications after doing PD such as pancreatic fistula (POPF), bleeding, and delayed gastric empty. Among them, POPF and bleeding have still been big problems [14, 15].

Postoperative Pancreatic Fistula

Postoperative pancreatic fistula (POPF) after LPD was reported at approximately 20% on average [14, 15]. POPF is defined and classified belong to the International Study Group for Pancreatic Surgery (ISGPS) 2016 [16]. There are different clinical conditions from asymptomatic to life-threatening patients. It may lead to further complications as inadequate management, for example, abdominal abscess, internal bleeding, wound infection, sepsis, and mortality.

The important key to treat POPF is to recognize this problem early and to prevent life-threatening sequela of this. An abdominal contrast-enhanced CT scan is necessary to assess

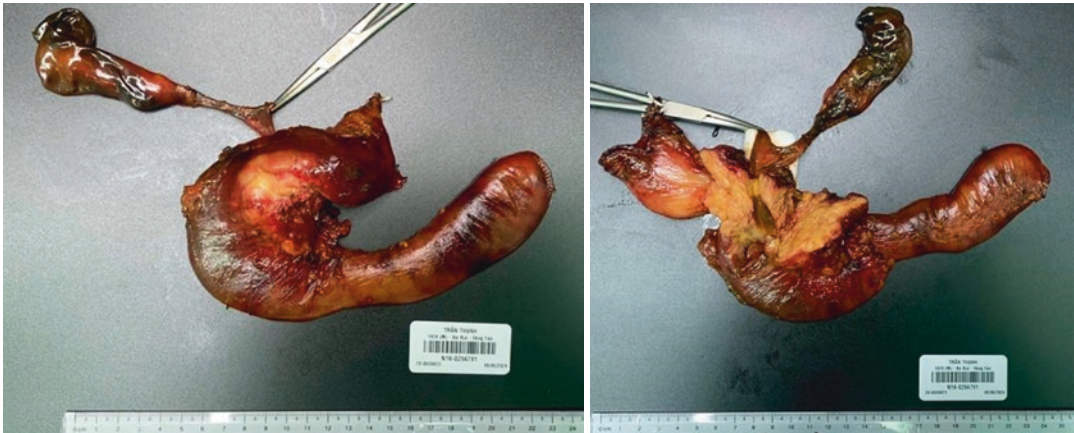


Fig. 18 Specimen

pancreatic anastomosis, fluid collections, signs of infected fluids, and intra-abdominal abscess.

Enteral nutrition is demonstrated to associate with higher rate of spontaneous fistula closure than parenteral nutrition in POPF patients. In pancreatojejunostomy where anastomosis is isolated from alimentary tract, oral diet is recommended although fistula is occurring.

Most POPF cases with stable clinical signs are treated by nonreoperation. The drains bringing well intra-abdominal fluids are remained and observed carefully. In case of fluid collection or intra-abdominal abscess, percutaneous or endoscopic ultrasonographic intervention is recommended.

Reoperation is indicated for sepsis shock, preventing sepsis or septic shock. Another indication of surgery is infected collection that requires lavage. Choice of open or laparoscopic surgery as reoperation depends on certain situation and surgeon's experience.

Bleeding

According to ISGPS [17], definition of hemorrhage after PD, called post-pancreatectomy hemorrhage (PPH), is based on three criteria: onset, location, and severity. Regarding onset, hemorrhage is defined as early and late PPH happening in less or more than 24 h, respectively. Turning to location, PPH is defined intraluminal (intra-enteric) and extraluminal (extra-enteric). Finally, we have mild and severe PPH. Based on

these criteria, PPH is classified into grade A, grade B, and grade C.

Being similar to POPF, PPH in patients who remain clinically stable is treated by angiographic intervention. Reoperation is needed for catastrophic hemorrhage that requires rapid gaining of hemostasis.

Summary

PD can be done feasibly by totally laparoscopic surgery. It includes dissection phase and reconstruction phase. However, this is a technically difficult procedure. Both require surgeons with advanced laparoscopic skills and experience in pancreatic surgery. Although outcomes are significantly improved in recent years, the complication rate is still high and management is still difficult.

References

1. Whipple AO, Parsons WB, Mullins CR. TREATMENT OF CARCINOMA OF THE AMPULLA OF VATER. *Ann Surg.* 1935;102(4):763–79.
2. Gagner M, Pomp A. Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc.* 1994;8(5):408–10.
3. Tol JA, Gouma DJ, Bassi C, Dervenis C, Montorsi M, Adham M, et al. Definition of a standard lymphadenectomy in surgery for pancreatic ductal adenocarcinoma: a consensus statement by the international

- study group on pancreatic surgery (ISGPS). *Surgery*. 2014;156(3):591–600.
4. Bassi C, Falconi M, Molinari E, Mantovani W, Butturini G, Gumbs AA, et al. Duct-to-mucosa versus end-to-side pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: results of a prospective randomized trial. *Surgery*. 2003;134(5):766–71.
 5. Berger AC, Howard TJ, Kennedy EP, Sauter PK, Bower-Cherry M, Dutkevitch S, et al. Does type of pancreaticojejunostomy after pancreaticoduodenectomy decrease rate of pancreatic fistula? A randomized, prospective, dual-institution trial. *J Am Coll Surg*. 2009;208(5):738–47. discussion 47–9
 6. Clerveus M, Morandeira-Rivas A, Picazo-Yeste J, Moreno-Sanz C. Pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy: a systematic review and meta-analysis of randomized controlled trials. *J Gastrointest Surg*. 2014;18(9):1693–704.
 7. El Nakeeb A, El Hemaly M, Askr W, Abd Ellatif M, Hamed H, Elghawalby A, et al. Comparative study between duct to mucosa and invagination pancreaticojejunostomy after pancreaticoduodenectomy: a prospective randomized study. *Int J Surg (London, England)*. 2015;16(Pt A):1–6.
 8. Hallet J, Zih FS, Deobald RG, Scheer AS, Law CH, Coburn NG, et al. The impact of pancreaticojejunostomy versus pancreaticogastrostomy reconstruction on pancreatic fistula after pancreaticoduodenectomy: meta-analysis of randomized controlled trials. *HPB*. 2015;17(2):113–22.
 9. Hua J, He Z, Qian D, Meng H, Zhou B, Song Z. Duct-to-mucosa versus invagination Pancreaticojejunostomy following Pancreaticoduodenectomy: a systematic review and meta-analysis. *J Gastrointest Surg*. 2015;19(10):1900–9.
 10. Keck T, Wellner UF, Bahra M, Klein F, Sick O, Niedergethmann M, et al. Pancreatogastrostomy versus pancreaticojejunostomy for RECONstruction after PANcreatoduodenectomy (RECOPANC, DRKS 00000767): perioperative and long-term results of a multicenter randomized controlled trial. *Ann Surg*. 2016;263(3):440–9.
 11. Liu FB, Chen JM, Geng W, Xie SX, Zhao YJ, Yu LQ, et al. Pancreaticogastrostomy is associated with significantly less pancreatic fistula than pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: a meta-analysis of seven randomized controlled trials. *HP*. 2015;17(2):123–30.
 12. Menahem B, Guittet L, Mulliri A, Alves A, Lubrano J. Pancreaticogastrostomy is superior to pancreaticojejunostomy for prevention of pancreatic fistula after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. *Ann Surg*. 2015;261(5):882–7.
 13. Xiong JJ, Tan CL, Szatmary P, Huang W, Ke NW, Hu WM, et al. Meta-analysis of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. *Br J Surg*. 2014;101(10):1196–208.
 14. Liao CH, Wu YT, Liu YY, Wang SY, Kang SC, Yeh CN, et al. Systemic review of the feasibility and advantage of minimally invasive Pancreaticoduodenectomy. *World J Surg*. 2016;40(5):1218–25.
 15. Chen K, Liu XL, Pan Y, Maher H, Wang XF. Expanding laparoscopic pancreaticoduodenectomy to pancreatic-head and periampullary malignancy: major findings based on systematic review and meta-analysis. *BMC Gastroenterol*. 2018;18(1):102.
 16. Pulvirenti A, Ramera M, Bassi C. Modifications in the international study Group for Pancreatic Surgery (ISGPS) definition of postoperative pancreatic fistula. *Trans Gastroenterol Hepatol*. 2017;2(12):107.
 17. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, et al. Postpancreatectomy hemorrhage (PPH)—an international study Group of Pancreatic Surgery (ISGPS) definition. *Surgery*. 2007;142(1):20–5.

Open Access This chapter is licensed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.

The images or other third party material in this chapter are included in the chapter's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the chapter's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

