Laparoscopic Pancreatic Resections for Cancer: Pushing the Boundaries

Mallika Tewari¹

Received: 16 October 2015 / Accepted: 20 October 2015 / Published online: 29 October 2015
© Association of Surgeons of India 2015

Abstract Laparoscopic pancreatic resection (distal pancreatectomy, pancreaticoduodenectomy, including pancreaticoduodenectomy with vascular resections) for pancreatic ductal adenocarcinoma is a technically demanding procedure, and the available evidence from selected high-volume centers suggest it to be well within the oncological principles of surgery for cancer, though this remains to be proven in a randomized study. This review summarizes the present status of laparoscopic resections for pancreatic cancer.

Keywords Laparoscopic distal pancreatectomy · Laparoscopic pancreaticoduodenectomy · Pancreatic ductal adenocarcinoma · Outcome · Survival

Introduction

Ever since laparoscopy took surgical practice with a storm in the late 1980s, it has become established as a *standard of care* for several general surgery procedures. Laparoscopic approach is gradually replacing “standard open approaches” in areas hitherto considered “no go” areas for laparoscopy—pancreatic cancer is one such field.

Why Laparoscopic Surgery?

The advantages of laparoscopic surgery are a smaller incision, reduced blood loss, superior magnified vision, shorter hospital stay, quicker/uncomplicated recovery and improved quality of life. Efforts are being made to reap these advantages for pancreatic procedures although with much less enthusiasm compared to cholecystectomy and colectomies. This could be due to the inherent risk of postoperative pancreatic fistula (POPF) formation and intimate relationship of the pancreas with large caliber vessels such as the portal vein (PV), superior mesenteric vein (SMV), superior mesenteric artery (SMA) and celiac axis. Another limiting factor is that such complex procedures require use of state-of-the-art technology and advanced laparoscopic skills over and above mastery in open surgery. Even experienced laparoscopic surgeons admit of having a learning curve for arduous laparoscopic pancreatic resections such as total laparoscopic pancreaticoduodenectomy (TLPD).

Laparoscopic Distal Pancreatectomy

The evolution of laparoscopic pancreatic surgery has been slow and initially involved resections without the need for any reconstruction such as for pancreatic necrosectomy and distal pancreatectomy (DP) $\pm$ splenectomy. Gagner and Cuschieri were the first to report laparoscopic distal pancreatectomy (LDP) in 1996 [1, 2], following which several small series were published indicating good short-term outcomes of LPD in benign lesions of the pancreas.

Kooby et al. in 2008 (Central Pancreas Consortium) published the first large, comparative, multicenter, matched, cohort study (8 centers) of LDP ($n=142$) versus open distal pancreatectomy (ODP) ($n=200$) [3]. They found no significant differences in operative time (216 vs. 230 min; $P=0.3$),

✉ Mallika Tewari
drmtewari@gmail.com

¹ Department of Surgical Oncology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, U.P., India

POPF (18 vs. 11 %; $P=0.1$), major complication (17 vs. 10 %; $P=0.08$), or 30-day mortality (1 vs. 0 %; $P=0.040$) between the groups (ODP vs. LDP, respectively). As compared to ODP, LDP was associated with lower estimated blood loss (357 vs. 588 mL; $P<0.01$), a higher rate of splenic preservation (30 vs. 12 %; $P<0.001$), fewer wound infections (5 vs. 15 %; $P=0.004$), a reduced need for postoperative percutaneous drain placement (6 vs. 15 %; $P=0.02$) and shorter hospital stays (5.9 vs. 9.0 days; $P<0.01$).

Since then, many more studies have been published highlighting the feasibility of LDP; of these, the most recent is a large, multicenter (69 medical centers) study by Nakamura et al. as a project of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JHBPS) [4]. Two thousand and ten patients (after exclusions) who underwent distal pancreatectomy from 2006 to 2013 were divided into two groups, ODP ($n=1108$) and LDP ($n=902$). Interestingly, this group from Japan used a sophisticated statistical method (propensity score matching (PSM)) for comparative analysis that attempts to recreate a randomized trial using observational data. A major caveat is however that the authors excluded invasive pancreatic cancer from their analysis, apparently the most challenging aspect of LPD.

After PSM (total patients 1458, with 729 patients in each group), LDP was found to be associated with lower blood loss (254 ± 384 vs. 499 ± 740 , $P<0.001$), fewer intra-operative blood transfusion rates (4 vs. 6.8 %; $P=0.02$), fewer grade B and C POPF (18.4 vs. 28.2 %; $P<0.001$), higher splenic preservations (29.9 vs. 13.2 %; $P<0.001$), and shorter hospital stays (18.8 ± 14.7 vs. 23.2 ± 18.8 ; $P=0.001$) but longer operating times (319 ± 129 vs. 261 ± 119 min; $P<0.001$).

Data regarding LPD for adenocarcinoma is slowly emerging. Still, the outcomes are not well defined in terms of oncological safety, and existing reports address few patients.

The Mayo Clinic, Rochester group reported their data comparing LPD ($n=100$ patients) and OPD ($n=100$ patients) matched by age, pathologic diagnosis, and pancreatic specimen length from their institution [5]. It included 23 patients with malignant pancreatic lesions in each arm. Pancreatic adenocarcinoma was the commonest malignant tumor (LDP, $n=17$; ODP, $n=19$), followed by neuroendocrine carcinoma (LDP, $n=3$; ODP, $n=2$) and metastatic renal cell carcinoma (LDP, $n=3$; ODP, $n=2$). A R0 resection was performed in all cases, and there was no difference in the number of lymph nodes harvested.

A recent meta-analysis published results of 5 comparative case control studies involving 261 patients (30.7 % LPD and 69.3 % OPD) with pancreatic ductal adenocarcinoma (PDA) [6]. The R0 resection rate, mean harvested lymph nodes, morbidity, POPF, reoperation, mortality, number of patients eligible for adjuvant therapy, and overall survival were found to be similar between the two groups. However, the LPD group had longer operative times ($P=0.04$), lesser blood loss ($P=0.01$), a

shorter hospital stay ($P<0.001$), and smaller tumor size ($P=0.04$) as compared to the OPD group.

Despite the lack of level 1 evidence, more centers are adopting LPD and report good outcomes although most opine that multicenter trials are needed to correctly evaluate the laparoscopic approach in PDA.

Total Laparoscopic Pancreaticoduodenectomy

Pancreaticoduodenectomy (PD) is a major abdominal surgery even when done by laparotomy as it requires extensive retroperitoneal dissection around anatomically complex and hazardous structures and a tedious reconstruction that includes 3 technically demanding anastomoses. TLPD is particularly challenging for it undoubtedly requires advanced laparoscopic skills, dexterity in suturing techniques and of controlling hemorrhage laparoscopically should an inadvertent injury occur of the porto-mesenteric axis, long operating hours (at least initially), has a learning curve and uncertain benefits. Although first reported by Gagner and Pomp in 1994, it was met with much pessimism [7]. This was followed by reports on a few patients undergoing hybrid procedures such as hand assisted or laparoscopic resection with open reconstruction [8, 9]. This severely limits assessment of the true value of a laparoscopic procedure.

Kendrick et al. from the Mayo Clinic in 2010 [10] reported a large, single institution series on feasibility of TLPD on 62 patients. Half of these patients ($n=31$) had PDA, 12 intraductal papillary mucinous neoplasm, 8 periampullary adenocarcinoma, 4 neuroendocrine carcinoma, 1 cholangiocarcinoma, 1 metastatic renal cell carcinoma, 1 cystadenoma, 1 duodenal adenoma, and 3 chronic pancreatitis. The median tumor size was 3 cm (range, 0.9–10 cm), and the median number of lymph nodes retrieved was 15 (range, 6–31). In all, 89 % of patients had an R0 (margin-negative) resection. POPF occurred in 11 patients, delayed gastric emptying in 9, bleeding in 5, and there was 1 postoperative mortality. Median length of hospital stay was 7 days (range, 4–69 days). The operative times dropped from a mean of 7.7 h in the first 10 patients to 5.3 h in the last 10 (mean 368 min; range, 258–608 min). The authors though optimistic about the feasibility of TLPD were skeptical of drawing any conclusions on the oncologic outcomes (such as tumor recurrence, disease-free and overall survival) due to the insufficient number of patients and length of follow-up.

Assessing for the *Oncologic Advantages Over Open Approaches*, the Mayo Clinic group from Rochester recently published data for all patients undergoing TLPD ($n=108$) or OPD ($n=214$) for PDA at their institution between January 2008 and July 2013 [11]. The TLPD group had a significantly ($P<0.001$) shorter hospital stay (6 days; range, 4–118 days) versus OPD group (9 days; range, 5–73 days). There was no

significant difference in the overall survival ($P=0.12$) after a median follow-up of 16.5 and 15.1 months in the LPD and OPD groups, respectively. Overall, 46 patients (43 %) in the TLPD group and 113 patients (53 %) in the OPD group developed recurrence. Interestingly, local recurrence was significantly less in the TLPD group (15 %) compared to the OPD group (27 %) ($P=0.04$) despite similar margin status after resection. Significantly, ($P=0.04$) more patients in the OPD group (12 %) had delayed adjuvant treatment (>90 days) or no adjuvant treatment at all compared to that in the TLPD group (5 %). A longer progression-free survival seen in the TLPD group could be because of reduced immunologic and physiologic impact of minimally invasive approaches and the enhanced recovery of TLPD patients enabling them to receive adjuvant treatment in a timely and complete fashion. This is thus one large, single institution study from a high-volume center that has shown results favoring TLPD in patients with PDA.

Even major vascular resections of the PV/SMV in the TLPD have been reported from the Mayo Clinic, Rochester, showing both feasibility and oncologic safety of these procedures in the exceptionally trained dexterous hands [12, 13].

Kendrick et al. published the first study describing the technique and outcomes of a series of 11 patients undergoing TLPD with major venous resection and reconstruction [12]. Ten patients underwent a tangential venous resection with a bovine pericardial patch repair in 4 (when 25–50 % of the circumference was found involved), and only one required segmental resection of the PV/SMV with left renal vein interposition graft reconstruction (Figs. 1 and 2). The mesoportal clamp time ranged from 10 to 82 (overall median 35) minutes. It is longer than in the open approach possibly representing their learning curve in laparoscopic venous resection. The extensive experience required (in OPD with vascular resection, TLPD, practice on animal model) before embarking on such advanced laparoscopic procedures cannot be overemphasized. Dr. Kendrick has summarized his surgical tips in Table 1.

Fig. 1 Intra-operative photo of patch venorrhaphy after tangential venous resection (Reproduced with permission from [12])

Fig. 2 Intra-operative photo of distal venous anastomosis using an autologous left renal vein interposition graft after segmental venous resection (Reproduced with permission from [12])

Robotic Pancreatic Surgery

It is believed, though highly debatable, that robotic technology offers a platform for superior 3D visualization and enhanced dexterity enabling complex dissections in difficult areas. A few studies from high-volume centers have reported that robotic pancreatic resections (DP and PD) are superior to LDP and TLPD. There seems to be fewer conversions to open, less blood loss, higher lymph node yield, and R0 resection rates [14–17]. One of the largest studies supporting the feasibility and safety of robotic pancreatic

Table 1 Surgical tips by Dr. M.L. Kendrick, Mayo Clinic, Rochester

(a) Laparoscopic pancreaticoduodenectomy: pearls for the open surgeon

- Magnification:
 - Enhances dissection and reconstruction
 - Most notable for uncinate and pancreaticojejunostomy (PJ)
- Equipment:
 - Ligasure for uncinate and small bowel mesentery
 - Reduces bleeding (?) and operative time
- Umbilical tape:
 - Enhances dissection and retraction
 - Allows “no-touch” technique

(b) Pearls for those just starting laparoscopic pancreaticoduodenectomy

- Acquire proficiency in open procedures and advanced laparoscopic skills!
 - Suturing skills a must
- Observe in the operating room not just a video!
 - Set-up and exposure is everything
- Patience is a virtue!
 - The first 10 cases are most difficult (don’t quit!)
 - Consider laparoscopic resection, open reconstruction
 - Start with pancreatic lesions having a dilated pancreatic duct, hard pancreas

resections was published by Zureikat et al. [17] from Pittsburgh wherein they analyzed and reported their data on 250 consecutive robotic pancreatic resections (PD 132, DP 83, central pancreatectomy 13, pancreatic enucleation 10, total pancreatectomy 5, Appleby resection 4, and Frey procedure 3). Giulianotti et al. published their series of patients undergoing robotic extended pancreatectomy and vascular resections without any conversions and mortality [18]. The robotic technique has certain shortcomings too like absence of haptic feedback, docking-undocking time, and the associated costs hindering widespread use.

Meta-analysis: Minimally Invasive Pancreaticoduodenectomy Versus OPD

A recent meta-analysis [19] (Table 2) of the existing (6 retrospective) studies [20–25] revealed certain advantages of minimally invasive pancreaticoduodenectomy (MIPD) over OPD (trend toward fewer wound infections, lower operative blood loss, shorter hospital stay, improved lymph node harvest, lower likelihood of R1 resection but longer operative times). The authors point to the likelihood of patients selected for laparoscopic approach for having smaller tumors and consequently relatively easier dissection, less blood loss, and more R0 resection rates. The fact that length of hospital stay is affected not only by the morbidities associated with these procedures

but also by local preferences and different health care systems cannot be denied. Similarly, the role of pathologists and the techniques used while assessing lymph nodes in the resected specimen and thereby affecting the overall lymph node count is important.

Another large analysis of the data on 7061 patients undergoing PD (983 MIPD vs. 6078 open) as identified from the National Cancer Database, 2010–2011, revealed no differences between MIPD and OPD for adenocarcinoma after multivariate analysis in lymph node harvest, rate of positive surgical margins, length of stay, or readmissions [26]. However, patients undergoing MIPD had higher 30-day mortality compared to open surgery (odds ratio 1.87, confidence interval 1.25–2.80, $P=0.002$). This could be due to the fact that majority of hospitals (92 %) performing MIPD were low-volume hospitals (≤ 10 cases/2 years) underscoring the need to perform these complex operations in a high-volume center by high-volume surgeons.

Nevertheless, advocates of MIPD credit the superior views, magnification, excellent exposure, and positive intra-abdominal pressure (limiting low pressure venous bleeding) for a more detailed and precise lymphadenectomy and pancreatic resection.

Several intriguing questions hence remain: (a) Is a randomized trial required and is it ethical comparing patients undergoing OPD and LDP? (b) Is PD an operation that should be performed using minimally invasive techniques? [27]

Table 2 Meta-analysis of different outcomes variables

Variable	Studies included	Patients* MIS/open	OR/WMD	95 % CI	<i>p</i> value	I^2 , %
Operative time, min	6	169/373	131	43–218	0.003 [†]	96
Blood loss, mL	6	169/373	(–) 1460	(–) 2194–(–) 726	<0.001 [†]	95
Harvested lymph nodes	5	161/365	(–) 3.2	(–) 6.0–(–) 0.3	0.03 [†]	61
R1/R2 resection [‡]	6	121/253	0.4	0.20–0.80	0.007 [†]	0
Tumor size, cm	4	117/326	0.6	0.1–1.1	0.02 [†]	51
Overall complications	6	169/373	0.67	0.39–1.16	0.15	39
PF overall	6	169/373	1.11	0.68–1.83	0.67	0
PF clinically relevant	6	169/373	0.97	0.48–1.99	0.94	0
DGE	4	147/351	0.75	0.35–1.63	0.48	0
PPH	4	147/351	1.55	0.70–3.42	0.28	0
Wound infection	4	147/351	0.49	0.23–1.1	0.077	0
Reoperation	5	155/359	0.54	0.25–1.18	0.12	0
Hospital stay	5	139/343	(–) 3.7	(–) 6.8–(–) 0.5	0.02 [†]	78

Reproduced with permission from Elsevier [19]

DGE delayed gastric emptying, MIS minimally invasive surgery, OR odds ratio, PF pancreatic fistula, PPH post-pancreatectomy hemorrhage, WMD weighted mean difference

*Total number of patients evaluated in each category

[†] Significant statistical difference

[‡] Calculated over the number of patients with a malignancy

Clearly, these questions need to be addressed so as to be wiser as a surgeon in providing the best outcome (both short-term and long-term) to the patients suffering with diseases of the pancreas.

Conclusions

Laparoscopic pancreatic resections provide typical benefits of minimally invasive approaches, may hold a promise of improving quality of life, appears to maintain standards of oncological resection; further evaluation is indeed necessary to validate advantages, and the ultimate success of these approaches requires patience and adherence to established surgical techniques.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no competing interests.

References

- Gagner M, Pomp A, Herrera MF (1996) Early experience with laparoscopic resections of islet cell tumors. *Surgery* 120:1051–1054
- Cuschieri A, Jakimowicz JJ, van Spreeuwel J (1996) Laparoscopic distal 70 % pancreatectomy and splenectomy for chronic pancreatitis. *Ann Surg* 223:280–285
- Kooby DA, Gillespie T, Bentrem D, Nakeeb A, Schmidt MC et al (2008) Left-sided pancreatectomy: a multicenter comparison of laparoscopic and open approaches. *Ann Surg* 248:438–446
- Nakamura M, Wakabayashi G, Miyasaka Y, Tanaka M, Morikawa T et al (2015) Multicenter comparative study of laparoscopic and open distal pancreatectomy using propensity score-matching. *J Hepatobiliary Pancreat Sci* 22:731–736
- Vijan SS, Ahmed KA, Harmsen WS, Que FG, Reid-Lombardo KM, Nagorney DM, Donohue JH, Farnell MB, Kendrick ML (2010) Laparoscopic vs open distal pancreatectomy: a single-institution comparative study. *Arch Surg* 145(7):616–621
- Ricci C, Casadei R, Taffurelli G, Toscano F, Pacilio CA et al (2015) Laparoscopic versus open distal pancreatectomy for ductal adenocarcinoma: a systematic review and meta-analysis. *J Gastrointest Surg* 19(4):770–781
- Gagner M, Pomp A (1994) Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc* 8:408e410
- Kimura Y, Hirata K, Mukaiya M, Mizuguchi T, Koito K, Katsuramaki T (2005) Hand- assisted laparoscopic pylorus-preserving pancreatoduodenectomy for pancreas head disease. *Am J Surg* 189(6):734–737
- Wellner UF, Küsters S, Sick O, Busch C, Bausch D et al (2014) Hybrid laparoscopic versus open pylorus-preserving pancreatoduodenectomy: retrospective matched case comparison in 80 patients. *Langenbeck's Arch Surg* 399(7):849–856
- Kendrick ML, Cusati D (2010) Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience. *Arch Surg* 145(1):19–23
- Croome KP, Farnell MB, Que FG, Reid-Lombardo KM, Truty MJ, Nagorney DM, Kendrick ML (2014) Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? *Ann Surg* 260(4):633–638, discussion 638–40
- Kendrick ML, Sclabas GM (2011) Major venous resection during total laparoscopic pancreaticoduodenectomy. *HPB(Oxford)* 13(7):454–458
- Croome KP, Farnell MB, Que FG, Reid-Lombardo KM, Truty MJ, Nagorney DM, Kendrick ML (2015) Pancreaticoduodenectomy with major vascular resection: a comparison of laparoscopic versus open approaches. *J Gastrointest Surg* 19(1):189–194, discussion 194
- Zureikat AH, Hogg ME, Zeh HJ 3rd (2014) The utility of the robot in pancreatic resections. *Adv Surg* 48:77–95
- Daouadi M, Zureikat AH, Zenati MS, Choudry H, Tsung A et al (2013) Robot-assisted minimally invasive distal pancreatectomy is superior to the laparoscopic technique. *Ann Surg* 257(1):128–132
- Chen Y, Yan J, Yuan Z, Yu S, Wang Z, Zheng Q (2013) A meta-analysis of robotic-assisted pancreatectomy versus laparoscopic and open pancreatectomy. *Saudi Med J* 34(12):1229–1236
- Zureikat AH, Moser AJ, Boone BA, Bartlett DL, Zenati M, Zeh HJ 3rd (2013) 250 robotic pancreatic resections: safety and feasibility. *Ann Surg* 258(4):554–559, discussion 559–62
- Giulianotti PC, Addeo P, Buchs NC, Aylow SM, Bianco FM (2011) Robotic extended pancreatectomy with vascular resection for locally advanced pancreatic tumors. *Pancreas* 40(8):1264–1270
- Correa-Gallego C, Dinkelspiel HE, Sulimanoff I, Fisher S, Viñuela EF, Kingham TP, Fong Y, DeMatteo RP, D'Angelica MI, Jamagin WR, Allen PJ (2014) Minimally-invasive vs open pancreaticoduodenectomy: systematic review and meta-analysis. *J Am Coll Surg* 218(1):129–139
- Asbun HJ, Stauffer JA (2012) Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the accordion severity grading system. *J Am Coll Surg* 215:810e819
- Buchs NC, Addeo P, Bianco FM et al (2011) Robotic versus open pancreaticoduodenectomy: a comparative study at a single institution. *World J Surg* 35:2739e2746
- Chalikonda S, Aguilar-Saavedra JR, Walsh RM (2012) Laparoscopic robotic-assisted pancreaticoduodenectomy: a case-matched comparison with open resection. *Surg Endosc* 26:2397e2402
- Lai EC, Yang GP, Tang CN (2012) Robot-assisted laparoscopic pancreaticoduodenectomy versus open pancreaticoduodenectomy—a comparative study. *Int J Surg* 10:475e479
- Zhou NX, Chen JZ, Liu Q et al (2011) Outcomes of pancreatoduodenectomy with robotic surgery versus open surgery. *Int J Med Robot* 7:131–137
- Zureikat AH, Breaux JA, Steel JL et al (2011) Can laparoscopic pancreaticoduodenectomy be safely implemented? *J Gastrointest Surg* 15:1151e1157
- Abdelgadir Adam M, Choudhury K, Dinan MA, Reed SD, Scheri RP et al (2015) Minimally invasive versus open pancreaticoduodenectomy for cancer: practice patterns and short-term outcomes among 7061 patients. *Ann Surg* 262(2):372–377
- Kooby DA, Vollmer CM (2015) Laparoscopic versus open distal pancreatectomy: is a randomized trial necessary? *J Hepatobiliary Pancreat Sci* 22(10):737–739. doi:10.1002/jhbp.279