

Minimally invasive surgical techniques for pancreatic cancer: ready for prime time?

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Abstract

Background Minimally invasive surgical techniques for pancreatic cancer are being applied with increasing frequency. With support of the literature, the location of the tumor within the pancreas is the factor which determines if these techniques can be safely used routinely by pancreatic surgeons.

Methods Literature supporting minimally invasive techniques for all types of resections for pancreatic cancer was reviewed.

Results Multiple meta-analysis regarding laparoscopic distal pancreatectomy all support the routine use of laparoscopy for these lesions. There are several case series describing the safety and efficacious use of laparoscopy in pancreaticoduodenectomy, and results have been promising in these highly specialized centers.

Conclusions The location of the tumor within the pancreas remains the most critical factor in the use of laparoscopy as the standard of care. Lesions in the body and tail, which are readily resected with a distal or subtotal pancreatectomy should be performed laparoscopically unless there is a clear reason why not to do so. Lesions in the head of the pancreas have been shown to be removed safely and effectively with laparoscopy. However, the technical skills necessary and the ability to teach these to trainees are the limiting factors to widespread use. Further series are necessary to assess if the laparoscopic approach to pancreaticoduodenectomy will play a similar role as the one it plays in the surgical treatment for distal lesions.

Keywords Laparoscopy · Distal pancreatectomy · Pancreaticoduodenectomy · Pancreatic cancer

Introduction

Pancreatic cancer has significant prevalence and incidence within the USA and throughout the world. In 2012, there were an estimated 44,000 new cases of pancreatic cancer [1]. More striking is that fact that there were >37,000 deaths from pancreatic cancer in 2012, and its associated 5-year survival is a mere 6 %. The dismal prognosis is caused by the fact that approximately 50 % of patients have distant disease at presentation, and an additional 25 % present with locally advanced disease. Due to the stigma of the disease and the complexity of the surgical resection, of the remaining 25 % who are resectable at presentation, half of these patients are never seen by a surgeon, or refuse an operation [2].

The misconceptions surrounding pancreatic surgery and its associated morbidity are beginning to change. As surgical skill and post-operative management have become more sophisticated, the morbidity and mortality associated with pancreatic surgery has declined in the last several decades. Additionally, the use of minimally invasive surgical (MIS) techniques is making the perception of pancreatic resection less daunting for patients. For an array of surgeries on other organ systems, laparoscopic techniques are associated with decreased post-operative pain, less narcotic use, and typically a shorter hospital stay. Recent studies have shown that these tenets may be true for pancreatic surgery as well. An additional added benefit is being studied which specifically raises the question of whether laparoscopy may afford a better technical operation for certain cases of pancreatic cancer. When looking for surrogate oncologic markers, the laparoscopic approach

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has been associated with a decreased estimated blood loss, similar or increased lymph node harvest, and similar or increased rates of R0 resection. Furthermore, the faster recovery from these surgeries postulates the possibility of an earlier start on adjuvant therapy. It has also been shown in the past that open surgery suppresses the immune system by multiple mechanisms, and these effects appear to be much reduced with laparoscopy [3]. This may be another oncologic advantage of the laparoscopic technique.

While these advantages are initially theoretical, there have been many studies attempting to quantify the benefits of MIS for pancreatic cancer. Just as in real-estate, ‘location, location, location’ appears to be the critical factor in determining how feasible a laparoscopic resection would be. It now appears clear that lesions in the body and tail of the pancreas are better treated with a laparoscopic distal pancreatectomy (LDP) [4]. Even though this may be evolving to be the standard of care, the national trends in the USA have not caught up. When the NIS and NSQIP database was studied, laparoscopy was only utilized in 15–27 % of cases nationally [5].

Lesions located within the head, uncinate and neck of the pancreas represent a significant challenge to laparoscopic resection. There are an increasing number of centers offering laparoscopic pancreaticoduodenectomy (LDP) for resection of these lesions, with only several centers reporting their outcomes from a large volume of cases. The advantages of laparoscopic resection have been published, but the widespread use of laparoscopy for proximal lesions is not ready for universal adoption.

Distal pancreatectomy

Tumors within the body and tail of the pancreas can often be treated with distal or subtotal pancreatectomy. This

resection was the first type of pancreatic surgery to be performed laparoscopically for several reasons. First, the dissection is technically feasible with the skills that most surgeons performing advanced laparoscopy already have. Second, the dissection and exposure are similar to the open operation, making it easier to learn. Finally, there is no reconstruction performed after an LDP. All of these are reasons why the laparoscopic technique can be adopted by pancreatic surgeons without extensive advanced laparoscopic surgery experience.

Recently, there have been several meta-analyses of LDP published around the world. The results of these studies are summarized in Table 1. They have all revealed that MIS techniques are associated with decreased length of stay, similar or improved morbidity and equal oncologic outcomes. A group at Johns Hopkins recently published a meta-analysis of 18 studies which directly compared LDP with open distal pancreatectomy (ODP) [4]. The data analyzed included 1,814 patients—57 % who had an open resection and 43 % who underwent a laparoscopic resection. They showed that the LDP had a lower blood loss by 355 mL ($p < 0.001$) and a shorter hospital stay by 4.0 days ($p < 0.001$). In terms of outcomes, LDP was associated with a lower morbidity rate of 33.9 %, compared to 44.2 % in the ODP group, with an odds ratio of 0.73. Specifically looking at pancreatic fistulas, they analyzed the rates of grade B–C pancreatic fistulas, as defined by the International Study Group on Pancreatic Fistulas. They found no difference between the LDP group at 12.5 % versus the ODP group at 15.6 %. Furthermore, there were no differences in margin positive resection, operative time, or mortality.

Our experience at the Mayo Clinic Florida has been recently published to directly compare LDP versus ODP [6]. The analysis included 90 patients in the ODP group and 82 patients in the LDP group, both had similar

Table 1 Meta-analysis comparing laparoscopic and open distal pancreatectomy with regards to operative variables and outcomes

Author	No. of studies	No. of patients	Percent lap vs open	Length of stay (decreased), days	EBL (decreased), mL	Morbidity	Margins	Pancreatic fistula
Venkat et al. [4]	18	1,814	43 % LDP 57 % ODP	4	355	Decreased 0.73 OR	NR	Equal 12.5 vs 15.5 %
Sui et al. [13]	19	1,935	42 % LDP 58 % ODP	3.87	273	Decreased 0.7 OR	Equal	Equal 14.5 % vs 17.9 %
Jin et al. [14]	15	1,456	38 % LDP 62 % ODP	4.98	263	Equal	NR	Equal
Xie et al. [15]	9	1,341	37 % LDP 63 % ODP	2.71	NR	Equal	NR	Equal 12.5 vs 13.4 %
Pericleous et al. [16]	4	665	43 % LDP 57 % ODP	2.7	NR	Reduced 0.78	NR	Equal

EBL estimated blood loss, LDP laparoscopic distal pancreatectomy, NR not reported, ODP open distal pancreatectomy, OR odds ratio

comorbidities and indications for resection. The LDP was associated with significantly decreased estimated blood loss (EBL) (180 vs 880 mL; $p < 0.001$), and thus fewer transfusions (0.35 vs 2.5 units; $p < 0.001$). Additionally, patients undergoing LDP had a shorter ICU stay (0.1 vs 0.7 days; $p < 0.001$), and a hospital stay which was shorter by 4 days (4.3 vs 8.1; $p < 0.001$). Rates of grades B-C pancreatic fistulas in the LDP and ODP were similarly low (6 vs 10 %). From an oncologic perspective, our analysis of surrogate oncologic markers confirms LDP is effective. Between LDP and ODP groups, lymph node retrieval was similar (18.7 vs 14.5; $p = 0.15$). Furthermore, the percent R0 resection was equal (97 vs 94 %).

While the various studies and meta-analysis have looked at these surrogate markers of oncologic resection, there is still a lack of data on long-term oncologic outcomes. Hopefully future prospective studies reporting 5-year survival data will answer these questions.

The issue of cost is often reported as an obstacle in the adoption of LDP. Several reports from around the world have analyzed the costs in comparison between open and laparoscopic techniques. Fox et al. [7] from the Toronto General Hospital evaluated 42 LDP and 76 ODP cases with respect to cost. The cost associated with the operating room was similar (\$4,655 for the LDP vs \$4,510 for the ODP). Due to a shorter length of stay and less intensive ward costs, the total hospital cost was significantly cheaper in the LDP group (\$10,842 vs \$13,656). This study and others, show that overall cost is decreased for LDP and this should

be another factor to be considered in terms of increasing the utilization nationally.

Laparoscopic pancreaticoduodenectomy

The first description of LPD was in 1994 by Gagner and Pomp [8]. At that time, they reported that the surgery was technically feasible; however, as this experience was early, they questioned the technical advantages and the viability of the laparoscopic approach when compared to traditional open resection. The slow progression of this technique is related to the technical challenges of this surgery. It requires a meticulous dissection near the portal vein, both at the pancreatic neck and in removal of the uncinate process. Additionally, the reconstruction poses another challenge, with biliary and pancreatic ducts often <5 mm in size, and the complexity of laparoscopic suturing on the soft pancreatic parenchyma.

Palanivelu et al. presented the first large series of LPD in 2007, and were the first to propose that not only was it possible but there may also be advantages in comparison to open resection [9]. As pancreatic surgery has become more sophisticated, and MIS techniques have become more advanced, the last several years have seen an increase in the number of centers performing LPD and reporting their outcomes. In a review of the literature, there have been 7 published series of LPD including at least 30 patients. The outcomes of these studies are presented on Table 2. The

Table 2 Published studies of laparoscopic and robotic pancreaticoduodenectomy which included at least 30 patients

Author	Years	No. patients	Technique	OR time (min)	EBL (mL)	No. lymph nodes	R0 Resection (%)	DGE	Pancreatic fistula (%)	Length of stay (days)	Morbidity	Mortality (%)
Palanivelu et al. [17]	2009	75	Lap	357	74	14	97.4	NR	7	8.2	26 %	1.33
Kendrick et al. [18]	2010	65	Lap	368	240	15	89	15 %	18	7	42 %	1.60
Giulianotti et al. [11]	2010	60	Robotic	421	394	18	91.70	5 %	21	22	NR	3
Zeh et al. [19]	2012	50	Robotic	568	350	18	89	20 %	12	10	56 % (30 % Clavien 3–5)	2
Chalikonda et al. [20]	2012	30	Lap/Rob	476	485	13	100	3 %	7	10	30 %	3
Kim et al. [21]	2012	100	Lap	487	NR	13	100	2 %	6	11.5	25 %	1
Asbun et al. [10]	2012	53	Lap	541	195	23	94.90	11 %	1	8	46 % (24 % Clavien 3–5)	6

DGE delayed gastric emptying, EBL estimated blood loss, Lap laparoscopic pancreaticoduodenectomy, NR not reported, Robotic robotic pancreaticoduodenectomy

reports conclude that LPD is associated with a lower EBL compared to OPD. The rate of pancreatic fistula varies between 6–21 %, with each having a variable rate of grade A-B-C fistulas. While the morbidity ranges from 25–56 %, the majority are minor complications and mortality rate is equivalent to open resection. One of the downsides of the laparoscopic technique is the operative time; the average length of LPD is 453 min between the above mentioned studies.

In an attempt to directly compare the laparoscopic and open techniques, the experience at Mayo Clinic Florida has been recently published [10]. Over a 3-year period, 53 patients underwent LPD and were compared with 215 patients that underwent OPD over an overlapping 6-year period. There was a significant decrease in EBL in the LPD group, from 1,032 mL to 195 mL ($p > 0.001$). This correlated with fewer transfusions during the hospital stay. Additionally, the ICU stay was nearly 2 days shorter (3 vs 1.1; $p < 0.001$), and the length of stay was 4 days shorter (12.4 vs 8; $p < 0.001$). With respect to the outcomes of the surgery, the major morbidity rates were equal (24.7 vs 24.5 %), including the rate of pancreatic B-C fistula (9 vs 9.5 %), and delayed gastric emptying (15.3 vs 11 %).

Some centers use robotic assistance and feel that this improves their dissection and reconstruction during pancreaticoduodenectomy. The largest series includes 60 patients, and comparable outcomes [11]. The proponents of the robotic technique state that the main advantages are 3-D optics, increased range of motion and fine motor movements. However, the robotic technique also has several disadvantages, including the lack of haptic feedback, difficulty operating in multiple quadrants of the abdomen, and high cost of the system and maintenance. There have been no studies directly comparing robotic and laparoscopic approaches and no objective evidence of the advantages of the robotic-assisted technique over the laparoscopic technique. Furthermore it appears that the use of the robot even though it facilitates prompter learning of suturing skills, may actually limit the surgeon in training to achieve his/her potential by making him/her become dependent on the use of the robot for complex tasks.

From an oncologic perspective, LPD is at least as good, if not better than the open approach. The experience of Kendrick at the Mayo Clinic in Rochester was shown to have similar oncologic outcomes when comparing 129 open resections to 52 laparoscopic resections [12]. Both groups had an equal margin-negative resection (83 %), and an equivalent number of lymph nodes removed (17 vs 18). They also reported equal recurrence rates of 38 % for the open group and 32 % for the laparoscopic group. Additionally, the 2-year survival rates were no different (43 vs 36 %). The Mayo Clinic Florida also compared the two techniques with respect to oncologic outcomes [10]. In this

study, the rate of margin-negative resection was improved for those undergoing LPD (83 vs 95 %) but did not reach statistical significance. Granted there is a potential selection bias towards the laparoscopic approach, as those patients with vein invasion are more directed towards an open approach. There was a significant increase in lymph nodes in the LPD group (17 vs 23). Importantly, this was also the first study to show that there was also a trend towards more patients receiving adjuvant therapy (57 vs 76 %) and with less delay after surgery (64 vs 58 days).

Summary

Laparoscopic techniques for pancreatic surgery have surged in the last 10–15 years. While the outcomes continue to improve, and the oncologic benefits continue to be discovered, the question of laparoscopic pancreas surgery becoming the standard of care continues to evolve. The location of the tumor within the pancreas appears to remain the most critical factor in this discussion. Lesions in the body and tail, which are readily resected with a distal pancreatectomy, should be no doubt performed laparoscopically unless there is a clear reason why not to do so. Multiple meta-analyses have shown the laparoscopic approach to be a safe oncologic surgery with many advantages with respect to less blood loss, decreased length of stay, and decreased morbidity. Lesions in the head of the pancreas have been shown to be removed safely and effectively with laparoscopy, and may also have several oncologic advantages. However, the technical skills necessary, and the ability to teach these to trainees remain to be the limiting factors to widespread use.

Conflict of interest None of the authors have anything to disclose.

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