# A review on the role of laparoscopy in pancreatic cancer

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## Abstract

***Background :*** **Pancreatic cancer is the fourth leading cause of cancer death in the United States and leads to an estimated 227,000 deaths per year worldwide. Palliative and curative treatments are used for pancreatic cancer by laparoscopic or open techniques. The role of laparoscopy in pancreatic cancer is evaluated in this study.**

***Material and Methods :*** **Electronic databases, such as PubMed/MEDLINE and Google Scholar were searched to identify reports of trials for laparoscopic pancreatic surgery. Articles written in English including the maximum number of patients published between 2010 and 2014 were included.**

***Results :*** **Recent reports on laparoscopic surgery of the pancreas are encouraging and support the advantages of laparoscopy. Although large series have been reported for benign pancreatic tumors treated with laparoscopic procedures, only limited data are available for malignant lesions. Most of these studies are retrospective, but the results encourage laparoscopic procedures.**

***Conclusion :*** **Over the last decade laparoscopic pancreatic surgery has emerged as an alternative to open surgery with many advantages. There are limited data on about laparoscopic approach for the treatment of malignant lesions. The results are in favor of laparoscopy.** (Acta gastroenterol. belg., **2016**, 79, **233-238**).

**Key words** : distal pancreatectomy, laparoscopic pancreatic surgery, pancreatic cancer, pancreaticoduodenectomy.

## Introduction

Pancreatic cancer is the fourth most common cause of cancer-related mortality, and leads to an estimated 227,000 deaths per year worldwide (1). It is one of the most aggressive malignant tumors. Overall, prognosis is dismal with recent 5-year survival estimates merely 6% (2). The latest age-standardized relative survival rates of pancreatic cancer in England during 2005-2009 show that 17.4% of men are expected to survive their disease for at least one year, falling to 3.6% surviving five years or more. The survival rates are similar for women, with 19.1% and 3.8% (1). There are no early detection tests and most patients with localized disease have no recognizable symptoms or signs ; as a result, most patients are not diagnosed until late in their disease, after their cancer has metastasized to other organs (3). Unfortunately only 15%-20% of patients have resectable disease at presentation (4).

The pancreas is an organ located in the retroperitoneal space of the abdomen. It is found behind the stomach and in close proximity to the duodenum, liver, spleen, and major vasculature. So, pancreatic surgery has too many technical complexities and requires considerable expertise. Two general types of surgical treatment of pancreatic cancer are curative and palliative surgery. Complete surgical resection is the only potentially curative treatment for long-term survival (5). Both of these treatments can be applied by open or laparoscopic or robotic procedures.

The last two decades has seen an increase in the application of minimally invasive surgical procedures to pancreatic resection for benign and malignant diseases. Laparoscopy is used in pancreatic cancer for different purposes : diagnostic or therapeutic. It has initially been used only for staging pancreatic cancer (4). With diagnostic laparoscopy, we can localize the tumor and decide that it is resectable or not. Laparoscopic enucleation (LE), laparoscopic distal pancreatectomy (LDP), laparoscopic pancreaticoduodenectomy (LPD) or palliative interventions are therapeutic laparoscopic procedures for pancreatic cancer. As surgeons become more adept at advanced laparoscopy, there is increasing evidence demonstrating not only the safety and feasibility of laparoscopic pancreatic resection, but also potential advantages in postoperative recovery and equivalent oncological outcome (6).

## Material and Methods

This study focuses on the current evidence base for increasing use of laparoscopy in pancreatic cancer. A literature search was performed using PubMed/MEDLINE and Google Scholar to identify clinical studies about laparoscopic pancreatic surgery using the search term “laparoscopy,” “distal pancreatectomy,” “pancreaticoduodenectomy,” “laparoscopic staging,” and “comparative study”. Furthermore, the combinations of these terms were used. The term “*vs*” or “*versus*” was used to find comparative studies. Articles written in English including the maximum number of patients published between 2010 and 2014 were included. The final search was performed on October 10, 2015.

## Diagnostic Laparoscopy

Accurate staging of pancreatic cancer is essential for the treatment. Patient selection is important to plan appropriate therapy and avoid non-therapeutic laparotomy in patients with unresectable disease. According to expert

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consensus statement on the pancreatic cancer multidedector computed tomography (CT) is current state of the art imaging modality (7). Cuschieri *et al*. first established the role of laparoscopy in the diagnosis, staging and assessment of the resectability of suspected malignancy of the pancreas in 23 patients (8). Gaujoux *et al*. reported that laparoscopic staging allowed for the identification of sub-radiographic metastatic disease in 10%-15% of patients with radiographically resectable pancreatic cancer, and in almost 30% of patients with locally advanced disease (9). A study by White *et al*. evaluated 1045 patients who had undergone laparoscopic staging (LS) between 1995 and 2005. The yield of LS was 14% ; because of the improvement of the cross sectional imaging and evaluation (10). In a retrospective review of 63 patients, Karachristos *et al*. correlated serum CA 19-9 levels with intraoperative findings on staging laparoscopy. Patients with a high serum CA 19-9 antigen level were significantly more likely to have metastases identified upon laparoscopic exploration. No patient with a CA 19-9 level below 100 U/mL were found to have metastatic disease (11).

The yield of staging laparoscopy in patients with radiographically resectable pancreatic tumors decreases the inability to show locally advanced tumors and liver metastasis. The addition of ultrasound to laparoscopy increases the yields and accuracy of LS (12). Laparoscopic examination of pancreatic tumors allows direct visualization and along with laparoscopic ultrasonography (LUS), it can reveal intra-parenchymal liver metastases, small peritoneal metastases, and vascular invasiveness of the tumor giving us a clearer picture of the resectability of the cancer (13). However, LUS offers a possible solution allowing the surgeon to examine the liver, the porta hepatis, the portal vein, and superior mesenteric artery. Diagnostic laparoscopy with the use of ultrasound improves the accuracy of predicting resectability up to as high as 98% in some studies (14). Bemelman *et al*. staged 70 patients with pancreatic cancer with laparoscopy and LUS. In this staging study, the overall sensitivity and specificity for determining resectability was 67% and 96%, respectively. Also, unnecessary laparotomy was avoided in 14 patients (19%) and a surgical decision was changed in 18 patients (25%) using combination laparoscopy and LUS (15). As stated in a recent expert consensus statement, laparoscopic staging could be selectively used in locally advanced pancreatic cancer and in apparent resectable cancer localized in the pancreatic body or tail and larger than 3 cm with equivocal findings on CT scan or in the setting of a high CA 19-9 level (> 100-200 U/mL) (7). In the light of these findings, selective use of laparoscopy with LUS for staging in questionable unresectable cases seems to be rational.

## Laparoscopic Distal Pancreatectomy

Laparoscopic distal pancreatectomy (LDP) is the most commonly performed pancreatic resection using minimally invasive techniques (6) and it was first described by Cuschieri in 1994 (16). It is now increasingly performed as the better alternate approach for distal pancreatectomy in selected patients and experienced centers (5). LDP is associated with a significantly lower operative blood loss, higher rate of splenic conservation, less postoperative pain, improved postoperative recovery, and shorter length of hospital stay as compared to open distal pancreatectomy (ODP) (17-27). Also, LDP seems to be a safe and effective alternative in terms of operation time, perioperative mortality and morbidity, such as pancreatic fistula formation, fluid collections, postoperative bleeding, and surgical-site infections (18-26). Moreover, in appropriately selected patients, LDP is more cost-effective than ODP. The increased cost associated with LDP is offset by the shorter hospitalization (28). A summary of series that compare the preoperative, intraoperative, and postoperative factors and outcomes in LDP and ODP at their institutions is shown in Table 1.

The average rate of conversion to ODP is about 10%-20% (6,17-27) ; because of obesity, abdominal adhesions, difficulty localizing the lesion, large and proximal tumors, hemorrhage, organ injury, and concern for margin adequacy (17,22-24,29). Conversion to open surgery may also be associated with a greater risk of postoperative complications (23).

In analogy to the findings in colorectal surgery where the oncologic efficacy and equivalency of laparoscopic procedures is well established, similar findings are observed for LDP (30). A retrospective study of multicenter analysis of 212 patients undergoing LDP for adenocarcinoma supports these findings. Rates of margin positivity, number of harvested lymph nodes, number of patients with at least one positive node, and overall survival are equivalent to open surgery (17,18,23-25). According to another study by Nakamura *et al*., the number of nodes retrieved and the rate of microscopic infiltration of the resection margin were similar in both groups (31). A retrospective cohort study by Jayaraman *et al*. compared 343 patients. Oncologic outcomes including R0 negative margins (97% vs 96%, P = 0.76) and lymph node harvest (6 vs 7, P = 0.53) were equivalent (23). Patients undergoing LDP tended to have smaller size lesions (2.5-3.9 cm in LDP vs 3-4.5 cm in ODP) (17-27).

LDP may be performed with or without splenic preservation. Spleen-preserving distal pancreatectomy is preferred for benign diseases or non-invasive neoplasms as the need for lymph node retrieval is not as crucial (32). The main advantage to splenic preservation is to avoid the risk of overwhelming post-splenectomy infection, which has an annual incidence of 0.23%-0.42% per year and a lifetime risk of 5% (6). For malignancy, splenectomy is needed to avoid compromising surgical margins (32). The rate of spleen-preservation ranged from 15.5% to 44.2% in LDP and from 5.7% to 15.6% in ODP (29).

Although these studies are retrospective and lesions are small, LDP provides similar short- and long-term

Table 1. — **Comparison : laparoscopic distal pancreatectomy (LDP) versus open distal pancreatectomy (ODP). The results are shown as "LDP/ODP" with mean values**

| Study (Reference) | LDP/ ODP | Operation time (min) | Blood loss (cc) | Conversion rate (%) | Hospital stay | Pancreatic fistula (%) | Tumor size (cm) | Malignancy (%) | Margin positivity (%) | Lymph node harvest |
|---|---|---|---|---|---|---|---|---|---|---|
| Magge *et al*. (17) | 28/34 | N/A | 290/570 | 17.6% | 6/8 | 21/29 | 3.7/4.5 | N/A | 14/12 | 11/12 |
| Stauffer *et al*. (18) | 82/90 | 188/233[a] | 70/500[a] | 7.0% | 4/8[a] | 13/14 | 2/2.8[a] | N/A | 3/6 | 16.5/11[a] |
| Mehta *et al*. (19) | 30/30 | 188/226 | 294/729 | N/A | 8.7/12.6 | 16.7/13.3 | 3.8/4.3 | 23.3/23.3 | N/A | 8.4/13.8 |
| Fox *et al*. (20) | 42/76 | 304/281 | 375/375 | 11.9% | 5/7 | 28.5/13.1 | 2.9/3.5 | 4.8/2.6 | N/A | N/A |
| Butturini *et al*. (21) | 43/73 | 180/180 | N/A | 0% | 8/9 | 29.7/13.7 | 3.9/4.0 | 4.7/2.7 | N/A | N/A |
| Cho *et al*. (22) | 254/439 | NS | 24%/54% (> 300 cc) | 9.4% | 16%/54% (> 7 days) | 23/27 | 40%/58% (> 3.5 cm) | 9/29 | N/A | N/A |
| Jayaraman *et al*. (23) | 107/236 | 194/163 | 150/350 | 30.0% | 5/7 | 15/13 | 3/3 | 17/47 | 3/4 | 6/7 |
| DiNorcia *et al*. (24) | 71/192 | 250/270 | 150/900 | 25.3% | 5/6 | 11.3/14.1 | 2.5/3.6 | 12.7/38.5 | 2.8/13.0 | 6/8 |
| Kooby *et al*. (25) | 23/189 | 238/230 | 422/790 | 17.0% | 7.4/10.7 | N/A | 3.5/4.5 | 100/100 | 26/27 | 13.8/12.5 |
| Vijan *et al*. (26) | 100/100 | 214/208 | 171/519 | 4% | 6.1/8.6 | 17/17 | 3.3/4 | 23/23 | 0 | NS |

N/A, data not available ; a, median values ; NS : statistically non-significant between the two groups.

oncologic outcomes as compared with ODP. In conclusion, LDP is safe, effective and feasible procedure in patient with benign or low grade malignancies of pancreas and a suitable option for the management of pancreatic cancers of the body and tail in selected patients (5,33). But for the malignant lesions, additional researches and larger prospective trials are necessary to improve the results of procedure.

## Laparoscopic Pancreaticoduodenectomy

Total laparoscopic pancreaticoduodenectomy (LPD) has recently emerged as one of the most advanced laparoscopic procedures of surgery. First LPD was performed by Gagner and Pomp in 1994 to treat chronic pancreatitis. In this first case, the surgical procedure took about 600 minutes and the patient stayed in hospital 30 days (34). The complexity of the operation, anatomic challenges and necessity of reconstruction with major anastomoses (intestinal, biliary, and pancreatic) makes LPD technically more demanding than other laparoscopic procedures. Despite the known benefits of laparoscopy, acceptance of LPD has not been as widespread.

Concerns about complications such as pancreatic fistula or complexities of anatomy and technique caused the progression of LPD slowly. Improvements in technical equipment and experiences have been resulted the steady increase in the numbers of LPD procedure. However, utility of LPD is still controversial (35, 36). In a meta-analysis, Nakamura and Nakashima demonstrated that the rate of postoperative complications, such as pancreatic fistula and wound infection after LPD and open pancreaticoduodenectomy (OPD) were similar and there were no significant difference in overall morbidity and mortality. Even though, LPD had less blood loss and lower rates of transfusion. A significantly longer operation time was required for LPD than OPD because of complicated procedures, including reconstructions (31). In a single-center clinical study of 100 patients with benign or malignant pancreatic head lesions who underwent LPD ; Kim *et al*. showed that the operation time decreased 9.8 to 6.6 hours, complication rate decreased from 33% to 17%, hospital stay decreased from 20.4 days to 11.5 days in course of time. It shows that procedure has a learning curve (37). A summary of series that compare the preoperative, intraoperative, and postoperative factors and outcomes in LPD and OPD at their institutions is shown in Table 2.

Asbun *et al*. and Kuroki *et al*. compared their LPD and OPD cases and found that LPD resulted in significantly less blood loss and longer operation time. The average length of hospital stay for LPD varies between 8 and 25 (38-42). Asbun *et al*. (40) found that the length of stay was significantly shorter in LPD group compared to OPD group (8 days vs 12.4 days), whereas Zureikat *et al*. (42) did not (8 days vs 8.5 days). The rate of converting LPD to open ranges from 0%-15% (38-42). Common reasons for conversion were hemorrhage, portal vein bleeding, difficult dissection, adhesions, and vascular invasion of the tumor (38-40,42). The rate of pancreatic fistulas is an important postoperative outcome and reported in majority of series with ranges from 11%-48% *vs* 12%-42.8% (38-42).

A large review of 258 patients who had undergone LPD between 1994 and 2011 stated that LPD was safe and feasible in pancreatic head resections ; margin-negativity and lymph node retrieval rates were also similar with OPD (43). Croome *et al*. (39) and Zureikat *et al*. (42) did not observe a difference in the number of lymph nodes retrieved (18.5-21.4 in LPD *vs* 19.1-20.1 in OPD). Asbun *et al*. found that tumor size, TN stage, number of positive lymph nodes, and R0 resections were not significantly different in the two groups (40). However, LPD is associated with a significantly higher number of overall lymph nodes harvested, as well as lower lymph node ratio.

Table 2. — **Comparison : laparoscopic panceraticoduodenectomy (LPD) versus open panceraticoduodenectomy (OPD). The results are shown as "LPD/OPD" with mean values**

| Study (Reference) | LDP/ODP | Operation time (min) | Blood loss (cc) | Conversion rate (%) | Hospital stay | Pancreatic fistula (%) | Tumor size (cm) | Malignancy (%) | Margin positivity (%) | Lymph node harvest |
|---|---|---|---|---|---|---|---|---|---|---|
| Dokmak *et al*. (38) | 46/46 | 342/264 | 368/293 | 6.5% | 25/23 | 48/41 | 2.8/2.5 | 78.2/78.2 | 40/50 | 20/25 |
| Croome *et al*. (39) | 108/204 | 379/387 | 492/866 | 6.4% | 6/9[a] | 11/12 | 3.3/3.3 | 100/100 | 22.2/23.4 | 21.4/20.1 |
| Asbun *et al*. (40) | 53/215 | 541/401 | 195/1032 | 15% | 8/12.4 | 16.7/17.3 | 2.7/3.1 | 73.6/65.6 | 5.1/17 | 23.4/16.8 |
| Kuroki *et al*. (41) | 20/31 | 656/554 | 376/1509 | 0% | N/A | 45/39 | N/A | 70/74 | N/A | N/A |
| Zureikat *et al*. (42) | 14/14 | 338/287 | 300/400 | 14% | 8/8.5 | 36.0/42.8 | 2.2/3.6 | 85.7/100 | 0/8.3 | 18.5/19.1 |

N/A, data not available ; a, median values.

LPD is currently a feasible and safe procedure in selected patients, operated on by experienced hands. But there is no clear evidence in favor of LPD in postoperative major morbidity, mortality, recovery, and oncologic outcomes compared to OPD. So, LPD cannot be considered superior or standard at this time. Multicenter randomized controlled prospective studies with a large number of cases and long follow-up evaluation are needed to provide more reliable information in laparoscopic pancreatic surgery.

## Laparoscopic Enucleation and Central Pancreatectomy

Laparoscopic enucleation (LE) has gained popularity in treating small benign pancreatic neoplasms or low-grade malignant pancreatic tumors, especially located on the surface of the pancreas away from the pancreatic duct (6,30). The main advantage of this less invasive technique is good preservation of normal pancreatic endocrine and exocrine function. In this context, intraoperative ultrasound assessment is crucial to evaluate location and multicentricity of the primary tumor, relation to the main vascular structures and pancreatic duct, presence of liver metastases, suspicious lymph nodes, and ensuring that the tumor can be enucleated with negative margins (30,44). The most important disadvantage to this procedure is the risk of pancreatic fistula formation. A recent review by Kuroki *et al*. summarizes that the rate of pancreatic fistula ranged from 13%-38% (45). In addition, endoscopic pancreatic stent placement before the tumor enucleation can be effective and safe method to avoid of pancreatic duct injury and postoperative pancreatic fistula (44). Currently, LE is considered safe, feasible, and effective procedure in selected patients under the guidance of LUS with favorable oncological outcomes. However, it must not be forgotten that postoperative complication rates are not negligible.

Laparoscopic central pancreatectomy (LCP) is an alternative technique for small benign or low-grade malignant tumors of the neck and proximal body of the pancreas with the advantages of preserving the spleen and normal pancreatic function (46-48). Despite the central pancreatectomy has been performing with increasing frequency in recent years, LCP has been slow to gain popularity and is still a new one with very few cases in view of concerns about safety (47). The main reason for limited data on LCP is the technical difficulty of the surgical procedure (pancreaticoenteric reconstruction) (46). LCP has been reported to be associated with negligible mortality ; nevertheless, postoperative morbidity, consisting of pancreatic fistula is high (29%-46%) (47,48). Thus, the laparoscopic approach for central pancreatectomy is promising but more evaluation, experiences and long-time follow-up data are needed to identify its indications and technical possibilities, and to promote its use.

## Conclusions

Laparoscopic pancreatic resections are gaining in popularity as a result of improvements in technology and increasing laparoscopic surgical experience. Current evidence suggests that laparoscopic pancreatic surgery is technically feasible and provides benefits over open surgery including decreased blood loss, shorter length of hospital stay, reduced postoperative pain, and expedited time to functional recovery. As a result of the advancements in laparoscopic instrumentation, an increasing number of surgeons are applying minimally invasive techniques to manage both benign and malignant neoplasms of the pancreas. Currently laparoscopic pancreatic surgery remains a reasonable surgical option for benign disease and low-grade malignant tumors when performed by highly skilled laparoscopic surgeons in specialized centers. In the future, perhaps after oncologic safety has been well demonstrated, laparoscopic techniques can be recommended for pancreatic adenocarcinoma, as early results are promising. But now, most of these studies are retrospective, total number of patients included in the trials are fairly small, and follow-up period is relatively short. Further studies with larger sample size and long-term follow-up are needed.

## Conflicts of Interest

The authors have no conflict of interests to disclose.

## Authorship

All authors had access to the relevant data and a role in writing the manuscript.

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