

Laparoscopic pancreatic resection—a review

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Abstract: Contrary to many other gastrointestinal operations, minimal access approaches in pancreatic surgery have gained ground slowly. Laparoscopic distal pancreatectomy has gained wide acceptance. It is associated with reduced blood loss and shorter duration of stay (DOS) while oncologic results and morbidity are similar to open surgery. In recent years the number of laparoscopic pancreatoduodenectomies has also increased. While oncological outcome seems comparable to the open approach, operative times are longer while DOS and blood loss are reduced. One added advantage of the laparoscopic approach to pancreatic cancer seems to be that adjuvant treatment can start earlier. Minimal access total pancreatectomy, only reported in small numbers (mostly robot assisted), has also been shown to be feasible and safe. Enucleation (EN) of small pancreatic lesions is the most common tissue sparing resection. Although no reconstruction is necessary, the risk of pancreatic fistula is high, related to excision margins equal or smaller than 2 mm to the main pancreatic duct. Compared to the open approach, laparoscopic EN has shown comparable results in terms of morbidity, pancreatic function and fistula rate, with shorter operation times and faster recovery. Experience in robot assisted pancreatic surgery is increasing. However reports are still small in numbers, lacking randomization and mostly limited to dedicated centers. The learning curve for minimal access pancreatic surgery is steep. Low patient volume leads to longer DOS, higher costs and negatively impacts outcome.

Keywords: Minimal access surgery (MAS); pancreas; pancreatic resection; laparoscopy

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Introduction

In the last decades minimal access surgery (MAS) has gained wide spread use both for benign and malignant disease in gastrointestinal surgery (1). Oncological adequacy has been shown in a variety of indications, including colonic (2,3) and gastric cancer (4). Laparoscopic pancreatic surgery, however, has been slow to gain momentum. Since the first description of minimal access cases reported in 1994 (5), the proportion of laparoscopic pancreatic resections remains low: according to the US Nationwide Inpatient Sample database from 2000 to 2011, only 5% of all resections were

performed via a minimal access approach (6). However, with progress in laparoscopic equipment, increasing numbers of cases have been reported in all indications (6,7). Our aim was to review the literature concerning the major advances in minimal access pancreatic surgery.

Definitions

The International Study Group on Pancreatic Fistula (ISGPF) (8) defined postoperative pancreatic fistula (POPF) as “drain output of any measurable volume of fluid on or

Table 1 ISGPF grading of POPF (8)

Grade	A	B	C
Clinical conditions	Well	Often well	Ill appearing/bad
Specific treatment*	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)**	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Sepsis	No	Yes	Yes
Readmission	No	Yes/no	Yes/no

*, partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue and/or minimal invasive drainage;

** , with or without a drain *in situ*. ISGPF, International Study Group on Pancreatic Fistula; POPF, postoperative pancreatic fistula; US, ultrasonography; CT, computed tomographic scan.

after postoperative day 3 with amylase content greater than 3 times the serum amylase activity". Severity is graded from A to C (Table 1).

Distal pancreatectomy (DP)

DP accounts for about a third of all pancreatic resections (6). Indications include benign, pre-malignant and malignant lesions of the pancreatic body/tail such as chronic pancreatitis, endocrine tumors, intraductal papillary mucinous neoplasm (IPNM), pancreatic pseudocysts, mucinous and serous cystic neoplasia, metastases and also trauma with ductal injury (9-11).

MAS accounts for between 10.8% to 46.6% of DP (9,12,13). Several publications have found no statistically significant difference in operative times between laparoscopic DP (LDP) and open DP (ODP), ranging from 156 to 383 min and from 145 to 330 min in laparoscopic and open surgery, respectively (14-17). Conversion rate ranged from 0% to 34% (18,19), hemorrhage and failure to progress being the most common causes. Estimated intraoperative blood loss was found to be significantly lower in LDP (9,13,14,20,21).

Morbidity in LDP has been reported to range from 0% to 67% in single center studies (22,23). However, recent meta-analyses (9,18) described overall morbidity ranging from 34.0% to 37.4%. As morbidity is essentially related to POPF, one possible explanation for this wide range of morbidity may be the use of different definitions for POPF. Adhering to the ISGPF definition, systematic reviews have described the POPF incidence to range from 16.8% to 21.7% in LDP (9,11).

Similarly, reported mortality (range, 0.2–0.4%) (9,18) and reoperation rates (range, 2.1–6.0%) (18,24,25) did not

differ from outcomes after open surgery. In spite of a variety of closure techniques available (suture, stapler, sealant, mesh), at the present time there is no proof that one closure technique is better than the other (26-30). Spleen preserving LDP has been described to be safe and feasible (10,22) and has been reported in 18.2% (16) to 60.4% (31) of LDPs.

In their 2015 meta-analysis of 34 studies, Mehrabi *et al.* (9) described a statistically significant difference in time to first oral intake (0–1.3 days) and duration of stay (DOS) (0–3.8 days). Of note, DOS after DP seemed to be shorter in the United States compared to centers outside of the United States, which might be attributed to differences in health care systems (18). More recently, Shin and colleagues (12) confirmed these reductions in their single center, propensity matched analysis.

Resection margin status was also studied in the meta-analysis by Mehrabi *et al.* (9): four studies (32-35) reported comparable R0 rates in both groups (592 patients) (OR: 1.63; 95% CI: 0.65–4.07; P=0.29), while the rate of R1 resections was lower in the LDP group (520 patients) (OR: 0.34; 95% CI: 0.14–0.83; P=0.02) (19,34-36).

The mean number of lymph nodes harvested did not differ significantly between LDP and ODP (12 to 13.8 LDP vs. 10 to 12.5 ODP) (12,13). However, the median number (10, range, 1–64) of lymph nodes harvested in the ODP group in one report (12) was less than 12, the recommended number for adequate disease staging (37).

Shin *et al.* observed a median postoperative survival of 33.4 months in LDP vs. 29.1 months in OPD (P=0.025) (12). In contrast a multicenter study by Kooby *et al.* found considerably shorter survival (16 months) in both groups (13).

While low long-term survival rates are typical for pancreatic cancer, the difference in survival between these last two studies might be attributed to the differences in median tumor size (3.0 *vs.* 3.5 cm) as well as the type of (monocenter *vs.* multicenter) study.

Pancreatoduodenectomy (PD)

Due to the anatomical position in the retroperitoneal space, the vicinity to large vessels and the need for three critical anastomoses, PD is considered one of the most challenging operations in GI surgery. Laparoscopic pancreatoduodenectomy (LPD) was described first by Gagner *et al.* over 20 years ago (5), but since then has not gained widespread use, as it was considered even more difficult (*vs.* the open approach) with questionable benefits to patients (38). However, with the advance of laparoscopic techniques and improved equipment, the number of LPD performed is continuously rising, as demonstrated by an increase of 50% from 2000 to 2010 according to Tran and colleagues (39).

Several studies have attempted to compare the operative and oncologic characteristics of open and laparoscopic pancreatic head resections, but none were randomized (38–52). Mean operative times have been reported to be significantly longer in LPD, ranging from 452 to 541 min for LPD compared to 372 to 401 min in OPD (40–42), although one center reported non-significant differences (465±86 *vs.* 465±98 min, respectively) (43). On the other hand, similar to what was observed in LDP, intraoperative blood loss has been reported to be significantly lower in LPD (492.4±519.3 to 841.8±994.8 mL in LPD *vs.* 866.7±733.7 to 1,452.1±1,966.7 mL in OPD) (43–45). DOS was significantly shorter in several comparative studies (6 to 8 *vs.* 9 to 12.4 days, respectively) (40,43,44) whereas other studies (7,41) found no statistically significant difference. Conversion to open surgery was reported in 9.1% to 30.0% of cases, mostly due to venous invasion and intraoperative bleeding (7,44,46). Overall morbidity in LPD has been reported to range from 35–52%, however this difference was not found to be statistically significant between the surgical approaches (43,47,48).

Postoperative mortality was recorded to range from 3.2% to 8.8% in LPD *vs.* 3.4% to 5.7% in OPD, difference which was not statistically significant (7,39,40,43). The reported incidences of clinical relevant POPF (grades B and C) described in several studies were fairly similar, ranging from 6.3% to 11.0% (45,49) in LPD and 5% to 9% (40,43)

in open surgery. In their systematic review, Correa-Gallego *et al.* (44) described overall POPF rates of 21% (8% grade B and C) in LDP and 17% (7% grade B and C) in ODP. This is comparable with Boggi and colleagues (46), who found a 24.8% incidence (10.5% grade B and C) for POPF after LDP in their meta-analysis.

Given that the majority of PDs are performed for malignant or premalignant lesions (7,46,49), adequate oncological resection remains one of the key questions. The number of lymph nodes harvested has been reported to be similar (7,45) or even significantly higher in LPD (40,43,44) compared to PD. Comparisons of R0 resection rates showed that results between open and LPD did not differ significantly (7,40,43,45,50). Of note, however, margin status may not be the ideal parameter for comparisons because definitions of margin involvement vary and under-reporting of microscopic margin involvement has been described (51). Portal venous infiltration as such is not a contraindication for the LPD (52). Interestingly, Croome and colleagues (45) reported a significantly longer interval of progression free survival and a shorter median time to adjuvant chemotherapy in LPD. However, overall survival was not improved, consistent with what is generally observed in pancreatic cancer (43,49).

However, most results come from highly experienced centers for LPD and may not be generally applicable. Moreover, several studies (39,47,48) have indicated that the learning curve is steep, DOS is increased and total costs are higher in centers performing fewer PDs. According to Adam and colleagues in their analysis of 7,061 PD for cancer in the US from 2010–2011, 92% of LPD (14% of all PDs) were undertaken in hospitals performing 10 LPD or less over a 2-year period. They also found a significantly higher 30-day mortality rate in LPD compared to OPD, which was inversely correlated with the volume of LPD per hospital (7). This is in agreement with the OPD learning curves described by Tseng *et al.* (53) identifying a number of 60 interventions necessary for adequate experience.

Total pancreatectomy (TP)

TP is rarely performed, accounting for 5.4% to 6.7% of all pancreatic resections in high volume centers (54,55).

This may explain why only a few papers (56–60) with small numbers have been published on laparoscopic total pancreatectomy, and thus showing only that it was feasible and safe with apparently satisfactory oncologic outcome.

Parenchyma sparing resections

Parenchyma-sparing resections are indicated in small—benign or low grade malignant—lesions, thus reducing the risk of exocrine and endocrine insufficiency (61). Safety and feasibility of enucleation (EN) and middle pancreatectomy, the most common procedures performed laparoscopically, have been described (62–64).

Indications for parenchyma sparing approaches include mainly neuroendocrine neoplasms, serous cystadenoma and branch duct IPMN as well as solitary renal cell carcinoma metastasis (62,65,66). Depending on the location, tumor size should not exceed 3 to 4 cm in diameter for laparoscopic EN (67,68). Although EN does not include a reconstructive phase, the procedure is associated with a high risk for POPF. In their systematic review on 811 patients undergoing EN, Beger *et al.* found a 36.7% POPF rate, 16.3% of which were clinically relevant (ISGPF grades B and C) (64). A resection margin equal or less than 2 mm from the main pancreatic duct has been identified as a high risk factor for development of POPF (67).

Zhang and colleagues (61) found no difference between open and laparoscopic EN concerning preservation of pancreatic function, but described shorter operation time as well as lower intraoperative blood loss and faster recovery (in terms of time to first flatus and first oral intake; DOS) in the minimal access approach. A systematic review by Briggs *et al.* reported conversion rates ranging from 10.5% to 44.4% with a 29.3% POPF rate (31).

Robotic-assisted surgery

The first robotic-assisted pancreatic resections were reported in 2003 by Melvin *et al.* (69) for DP and by Giulianotti *et al.* (70) for PD. Since then several reports (71–73) have shown promising results, comparable to and at times better (conversion rate, DOS) than standard laparoscopy and open procedures. While most studies represent early experiences, there is a significant learning curve for robotic pancreatic surgery (74), as in other robotic-assisted procedures (75). Boone *et al.* (76) described a continuous learning effect with statistically significant improvement after 20 (conversion rate, blood loss), 40 (POPF incidence) and 80 (operative time) procedures.

Of note, the total cost per operation is higher in the robotic approach [\$8,304 robotic DP (RDP) *vs.* \$3,861 LDP; robotic PD +€6,200 *vs.* OPD] (77,78). Interestingly, however, in their single institution experience, Waters

et al. (36) reported lower overall costs for robotic DP after adjusting for DOS (\$10,588 RDP *vs.* \$12,986 LDP *vs.* \$16,059 ODP). Notwithstanding, hospital costs are most likely subject to substantial variations depending on different health care systems (79).

Conclusions

Laparoscopic pancreatic resections have been shown to be feasible and safe, with rising numbers being reported during the last decade. Most LPD have been performed in university and urban teaching hospitals, while DP seems to be more widely implemented (6).

Comparisons with open surgery have shown reductions in hospital stay and intraoperative blood loss as well as similar results in terms of oncological adequacy. However, none of the data included in this review derive from controlled randomized studies and often represent single center or even single surgeon's experience, thus underscoring a significant risk for bias. This stresses the need for RCTs wherever possible.

Another major issue is the steep learning curve associated with pancreatic surgery in general and specifically the minimal access approach. Low volume hospitals have been shown to be significantly associated with worse patient outcomes. Robotic assisted surgery is gaining popularity especially in the U.S.

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Footnote

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