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Review

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A narrative review of the history and recent advances in minimally invasive pancreatic resection

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Abstract

Pancreatic resections are complex operations that carry the potential for long-term and life-threatening complications. Over the past several decades, improved surgical techniques and perioperative care have decreased the morbidity and mortality associated with these operations. As laparoscopic and robotic-assisted surgery has been increasingly used in other specialties, the role of minimally invasive techniques in pancreatic surgery remains unclear. We aimed to review the evolution of pancreatic surgery and summarize current data comparing outcomes between open and minimally invasive pancreatic techniques. A comprehensive review was performed using MEDLINE/PubMed with the search dates of January 1, 2018 to February 28, 2023. In PubMed, the terms "pancreas", "minimally invasive surgery", and "robotic surgery" were searched. Minimally invasive distal pancreatectomy (DP) is associated with decreased length of hospital stay and intraoperative blood loss with similar morbidity and mortality when compared to open DP. While randomized data supports decreased length of stay for minimally invasive pancreaticoduodenectomy (PD), the LEOPARD 2 trial was terminated early due to increased mortality among patients undergoing laparoscopic PD. Minimally invasive DP appears safe and efficacious compared to open surgery, whereas additional ongoing randomized studies from experienced centers are needed to determine the role of minimally invasive surgery for PD.

Keywords: Pancreas, minimally invasive surgery, robotic surgery, open surgery

INTRODUCTION

The pancreas is a retroperitoneal organ responsible for both endocrine and exocrine functions in the body. Given its retroperitoneal location, surgery on the pancreas can be challenging as it is surrounded by many critical structures, such as the portal vein, superior mesenteric artery and vein, and duodenum, among others. Pancreatic adenocarcinoma (PDAC) is the most common indication for surgical resection of the pancreas and other malignancies such as ampullary, neuroendocrine, bile duct, and duodenal tumors. In addition, pancreatectomy may be indicated for benign etiologies, such as cysts, trauma, and pancreatitis[1-4]. Unfortunately, among cancer patients, only 15%-20% of them are potentially resectable at initial presentation[5].

Surgical resection of the pancreas, however, carries a high risk of perioperative morbidity and mortality. The post-operative potential sequelae of pancreatectomy, such as post-operative pancreatic fistula and delayed gastric emptying, among others, potentially impact both short- and long-term quality of life. While significant advances in surgical techniques and perioperative care have reduced mortality to less than 2% at experienced centers, morbidity after pancreatectomy remains high[6].

Operative techniques for pancreatectomy vary based on the location of the pathology. Lesions in the body or tail of the pancreas are amenable to distal pancreatectomy (DP), whereas lesions in the head and uncinate process often require pancreaticoduodenectomy (PD). Both procedures are complex and traditionally have been performed in an open fashion. In recent decades, however, the utilization of minimally invasive pancreatectomy has increased due to its reported benefits over an open approach, including reduced pain, decreased incidence of wound infection, and faster recovery. Herein, we present a narrative review of level 1 prospective randomized trials in the field of minimally invasive pancreas surgery compared to traditional open approaches. The aim of this review is to discuss the history and evolution of minimally invasive pancreas surgery and compare its safety and efficacy to open pancreatic surgery.

METHODS

We performed a comprehensive search strategy in the MEDLINE database for studies published between January 2018 through February 2023. The following keywords and Medical Subject Headings were included in our search: “pancreas”, “minimally invasive surgery”, AND “robotic surgery”. Records were excluded during screening if not written in English. Reports were not retrieved if the full text was not available. Three hundred thirty-four reports were assessed for eligibility and were excluded if they were meta-analyses (n = 15), reviews other than systematic (n = 87), or non-Level 1 data (n = 207). A total of 25 reports were included. Of these, five were clinical trials. All identified publications were reviewed for inclusion by two reviewers (AS and NMB), and inconsistencies were addressed by discussion and consensus among the reviewers.

History of techniques for open pancreatic surgery

The first radical resection of the duodenum and head of the pancreas was performed in a staged fashion by Drs. Whipple, Parson, and Mullins in 1934 for a patient with ampullary cancer. Unfortunately, the patient expired soon after the procedure due to anastomotic breakdown[7,8]. Six years later, Dr. Whipple completed the first one-stage PD for a patient with gastric cancer metastatic to the head of the pancreas[9]. In the interim, the first successful PD for PDAC was performed in 1937 by Alexander Brunschig[10]. The pylorus-preserving technique for PD was introduced in 1944, although it truly gained prominence in 1978 after Traverso and Longmire proposed that sparing the pylorus would reduce the incidence of postgastrectomy syndrome and marginal ulceration[11].

In the subsequent decades, techniques aimed at improving the original PD technique; however, the mortality rate for open PD was approximately 20%, with a perioperative morbidity rate between 40%-60% in the 1970s[12,13]. Perhaps the next most important discovery in pancreatic surgery was the improvement in outcomes by high-volume surgeons at high-volume centers. When performed in high-volume pancreatic centers, mortality rates following pancreatectomy decreased to less than 5%[14,15]. The benefits of performing pancreatectomy at high-volume centers include standardized evidence-based work-up, operative techniques, and post-operative management resulting in shorter operative times, decreased blood loss, and a subsequent improvement in outcomes[16,17].

Introduction of minimally invasive pancreatic surgery

As the techniques and perioperative management for patients undergoing pancreatectomy were refined, they were exclusively performed through a traditional open approach. For patients undergoing other abdominal and thoracic procedures, minimally invasive surgery was shown to decrease hospital length of stay (LOS) and surgical site infections and improve pain control[18].

The first laparoscopic PD was performed in 1994 for chronic pancreatitis by Drs. Gagner and Pomp[19]. However, given the lengthy complex operation of a pancreatectomy, the potential for increased cost, and the worry of inferior oncologic outcomes, adoption of minimally invasive techniques initially remained low for patients undergoing pancreatectomy. Additionally, the limited instrument range of motion, poor ergonomics, and steep learning curve to perform three high-risk anastomoses also caused slow adoption of laparoscopy for PD[19]. Conversely, laparoscopic DP was first performed in the early 1990s and was adopted far more readily as it does not require major reconstruction[20].

The advent of the da Vinci robotic surgical platform in the late 1990s was critical to the increased adoption of minimally invasive techniques for pancreatic surgery. Robotic surgery more closely mimics open surgery and provides the benefits of improved three-dimensional surgical field visualization, tremor reduction, and additional instrument degrees of freedom[21]. Indeed, the 3D vision during robotic PD has shown improvement in performance and reduced anastomosis construction time[22]. The first case of robotic DP was described in 2003 by Melvin *et al.* for a patient with a symptomatic pancreatic cyst, while Giulianotti *et al.* described the first experiences with robotic PD in the early 2000s[23,24]. While numerous retrospective studies have demonstrated equivalent morbidity and mortality between minimally invasive and open pancreatectomy, there are limited prospective data comparing these techniques[25-27]. The remainder of this review will focus on analyzing the recent literature comparing minimally invasive *vs.* open pancreatic surgery.

Recent trials on minimally invasive distal pancreatectomy

Completed trials

With the surge in minimally invasive surgical techniques, minimally invasive DP has been thoroughly studied over the past decade. The seminal trial was the LEOPARD trial, which was a multicenter patient-blinded randomized controlled trial conducted in the Netherlands between 2015 and 2017. Patients with left-sided pancreatic tumors confined to the pancreas without vascular involvement were randomized to either a minimally invasive (laparoscopic and robot-assisted) (n = 51) or open DP (n = 57). The primary outcome was time to functional recovery, defined as independent mobility, pain control with oral medication, and taking 50% of required caloric intake without intravenous fluids. The investigators found that a minimally invasive approach had a significantly shorter time to functional recovery (4 days *vs.* 6 days, respectively, P < 0.001), lower operative blood loss (P < 0.001), and decreased delayed gastric emptying grade B/C (P = 0.04) compared to an open approach. However, operative time was significantly longer for minimally invasive PD. There was no significant difference seen in Clavien-Dindo grade III or higher complication rates, post-operative pancreatic fistulas grade B/C, or 90-day mortality between open and minimally invasive approaches[28].

A follow-up study using the LEOPARD trial cohort evaluated long-term quality of life, cosmetic satisfaction, and overall major complications beyond one year[29]. After a median follow-up of 44 months for 84 patients, there was no significant difference between minimally invasive and open DP groups in the primary outcomes of quality of life, major complications, readmission, and incisional hernia. However, patients were more content with their cosmesis in the minimally invasive group.

The LAPOP trial followed the LEOPARD trial and was an unblinded single-center superiority study conducted between 2015 and 2019 in which patients were randomized to laparoscopic (n = 29) or open DP (n = 29). The primary outcome was the length of post-operative hospital stay, and secondary outcomes included time to functional recovery, operative time, and perioperative complication rates. Median post-operative hospital LOS (5 *vs.* 6 days in open; P = 0.002) and time to functional recovery (4 *vs.* 6 days; P = 0.007) were significantly shorter in the laparoscopic DP group compared to the open group. No difference was seen in operative time or complication rates between the two groups[30].

The LEOPARD and LAPOP trials represent the only two published randomized prospective trials to date, evaluating outcomes between minimally invasive and open techniques for DP. It is important to note that these trials included both benign and malignant indications for pancreatectomy and, therefore, did not compare oncologic outcomes between the two surgical approaches[31]. An individual patient data meta-analysis from the International Minimally invasive Pancreatic Resection Trialist Group (IMIPRT) compared outcomes in all patients from the LEOPARD and LAPOP trials[32]. The authors found similar rates of major complications between minimally invasive and open approaches (adjusted odds ratio 0.54; P = 0.148), although there was a trend toward higher pancreatic fistula in the minimally invasive group. They concluded that in properly trained hands, minimally invasive DP may be the preferred approach. The findings of the LEOPARD trial were further validated by an assessment of the National Quality Improvement Program of the American College of Surgeons (ACS-NSQIP), which showed an 11% risk reduction in composite major morbidity after minimally invasive DP compared to an open approach[33].

In addition to these two seminal trials, much has been published on minimally invasive DP compared to an open approach. A 2020 study randomized 60 patients to laparoscopic or open DP and found shorter LOS and time to recovery and less bleeding with laparoscopy[30]. There was no difference in complications, including pancreatic fistula. Another randomized controlled trial from 2023 showed improved quality of life in patients undergoing laparoscopic DP at two years post-operatively[34]. A European consortium performed a propensity score-matched study comparing oncologic outcomes for patients who underwent minimally-invasive *vs.* open DP between 2007 and 2015[35]. Overall survival, perioperative complications, and 90-day mortality were similar between groups; however, R0 resection was significantly higher in the minimally invasive group. Interestingly, despite the equivalent survival and oncologic outcomes, the number of lymph nodes harvested was lower in the minimally invasive group. Other retrospective, propensity-matched studies and meta-analyses have shown similar results[36-43]. However, one propensity-matched study from a Korean group showed improved overall and disease-free survival for minimally invasive DP compared to an open approach[44]. Additionally, in contrast to the majority of the literature, an assessment of the ACS-NSQIP database found higher rates of post-operative pancreatic fistula in the minimally invasive group, similar to the IMIPRT group study mentioned above[45]. This was validated by a randomized controlled trial by van der Heijde *et al.*, which showed higher rates of post-operative pancreatic fistula in the minimally invasive DP[46]. Further studies are needed to clarify these conflicting results regarding the impact of a minimally invasive on post-operative pancreatic fistula.

Most of these studies included only patients with PDAC. When comparing minimally invasive to open DP in patients with nonfunctioning pancreatic neuroendocrine tumors (PNET) specifically, long-term survival did not differ; however, a minimally invasive approach did result in significantly fewer lymph nodes harvested[47]. Another study retrospective cohort study utilizing propensity score-matching to compare minimally invasive and open DP for the treatment of PNET found less blood loss, complications, LOS, and five-year recurrence in the minimally invasive group[48]. Similar findings were seen in another multicenter comparative study; however, cost was listed as the major limitation of a robotic approach[49].

Another area of the intense study is comparing robotic *vs.* traditional laparoscopic approaches to DP. One of the first meta-analyses on the subject showed no difference in oncologic outcomes between the two methods, although robotic DP had longer operative times and increased 90-day readmission rates[50]. Another recent multi-institutional trial showed some benefits to robotic DP in terms of decreased rates of conversion to open, increased splenic preservation, and decreased readmission rates; however, it again showed longer operative time compared to laparoscopic DP[51]. A recent study by the European Consortium on Minimally invasive Pancreatic Surgery concluded robotic and laparoscopic DP provide comparable R0 resection rates and overall survival, but a robotic approach was associated with longer operative time[52]. These collective findings may indicate that operative times may be related to the platform itself and the learning curve of this approach[53].

Other techniques for minimally invasive DP have been studied, including the radical antegrade modular pancreatosplenectomy (RAMPS) approach. DP was traditionally done via a left-to-right surgical approach in which the spleen, tail, and body of the pancreas were fully mobilized, and then the pancreas was divided[54]. The RAMPS procedure has recently been popularized as an alternative to the traditional left-to-right approach. First reported in 2003 by Strasberg *et al.*, the RAMPS procedure involves dissection performed from right to left, with an early division of the pancreatic parenchyma and splenic vasculature[55]. By performing dissection in an antegrade fashion, the RAMPS procedures allow for improved visibility and procurement of lymph nodes, easier identification of superior mesenteric artery involvement, and achievement of negative margins compared to traditional left-to-right approaches[56,57]. Importantly, there was no increased risk of perioperative complication between the two techniques and even higher overall survival in patients treated with RAMPS[58-60].

With regards to a minimally invasive RAMPS, a recent systematic review evaluating laparoscopic RAMPS reported median R0 resection rates between 91%-100% and concluded laparoscopic RAMPS had acceptable oncologic outcomes and safety profile[61]. In comparison to an open approach, Zhang *et al.* subsequently performed a single-center retrospective study, which showed that laparoscopic RAMPS was safe and had equivalent oncologic outcomes[62]. Similarly, multiple recent meta-analyses have shown no differences in oncologic outcomes between minimally invasive and open RAMPS procedures, although some did note that significantly fewer lymph nodes were harvested in minimally invasive approaches[63-66]. When comparing laparoscopic RAMPS to laparoscopic DP using the traditional left-to-right approach, a recent 2022 study from Niu *et al.* showed laparoscopic RAMPS obtained more lymph nodes and trended towards improved overall survival, although this did not achieve statistical significance[67].

Ongoing trials on minimally invasive distal pancreatectomy

The DP, minimally invasive or open, for malignancy (DIPLOMA) trial is the first randomized controlled trial comparing minimally invasive (laparoscopic and robot-assisted) and open DP in patients exclusively with PDAC. This international randomized controlled, patient- and pathologist-blinded trial aims to enroll 258 patients to examine the primary outcome of negative microscopic resection margin (R0) and secondary outcome of survival following DP for PDAC. Results are still pending, with anticipated trial completion in 2025[31].

Two multicenter prospective randomized controlled trials in Asia are currently recruiting in Korea (NCT03957135) and China (NCT03792932). Both studies include patients with malignant pancreatic tumors of the body or tail and will be randomized to laparoscopic or open DP. The primary outcomes of these trials are two-year overall (Korea) and two-year disease-free (China) survival, with results expected in 2024-2025[68].

The DISPACT-2 is a German multicenter randomized controlled trial comparing minimally invasive (laparoscopic or robotic-assisted) and open DP for benign or malignant disease. The primary outcome is post-operative mortality and morbidity within three months post-operatively. Secondary outcomes include pancreatic-specific complications, oncologic outcomes, and patient-reported outcomes. Results are expected in 2024[69].

An ongoing multicenter randomized clinical trial by Dai *et al.*, the MIRROR trial (NCT03770559), is assessing the safety and efficacy of minimally invasive RAMPS by examining factors such as LOS, short-term outcomes, and survival[70]. A group from China is currently investigating robotic RAMPS *vs.* standard RAMPS for PDAC. In this randomized single-center trial, the investigators will assess rates of R0 resection, the number of lymph nodes harvested, perioperative complications, the duration of surgery, cost, and blood loss[71]. A list of ongoing trials comparing minimally invasive and open DP is shown in Table 1.

Recent trials on minimally invasive pancreaticoduodenectomy

Completed trials

Minimally invasive PD was less readily adopted than DP in part due to the complex reconstruction. There have been many studies comparing minimally invasive to open PD. A recent randomized controlled trial in 2021 by Wang *et al.* compared outcomes from 14 medical centers in 762 patients undergoing laparoscopic and open PD for pancreatic or periampullary tumors[72]. The primary outcome was post-operative LOS, which was significantly shorter for patients undergoing laparoscopic PD (laparoscopic LOS 15 days *vs.* open LOS 16 days). There was no difference in serious post-operative morbidities or comprehensive complication index scores between the two groups. The authors concluded that in high-volume centers, laparoscopic PD was a safe and feasible procedure.

The PLOT trial was a single-center randomized controlled trial conducted in India between 2013 and 2015, in which patients with peri-ampullary tumors were randomized to laparoscopic (n = 32) *vs.* open (n = 32) PD. The initial primary outcome was the perioperative complication rate; however, this was changed at interim analysis to the length of hospital stay in order to achieve an adequate sample size. Patients undergoing laparoscopic PD had a significantly shorter hospital stay (13 *vs.* 7 days, P = 0.001) and reduced blood loss but longer operative time compared to patients undergoing open PD. There was no difference seen in post-operative complications or oncologic outcomes between the groups[73].

The PADULAP randomized controlled trial was completed in Spain between 2013 and 2017 and compared perioperative outcomes of laparoscopic (n = 34) *vs.* open (n = 32) PD. Laparoscopic PD was associated with shorter hospital LOS (median 13.5 *vs.* 17 days), longer operative time, and decreased complication rates (all P < 0.05). There was no significant difference seen in pancreas-specific complications, the number of lymph

Table 1. Ongoing clinical comparing minimally invasive and open distal pancreatectomy

Trial name	Year registered	Anticipated completion date	Groups	Patient population	Primary end point
DIPLOMA ISRCTN44897265	2018	2025	MIDP *vs.* ODP	PDAC	R0 resection rate
NCT03957135	2019	2025	Laparoscopic DP *vs.* ODP	Resectable PDAC body or tail	2-year OS
NCT03792932	2019	2023	Laparoscopic DP *vs.* ODP	Resectable PDAC body or tail	2-year RFS
DISPACT-2	2020	2024	MIDP *vs.* OPD	Benign + malignant body or tail lesions	CCI 3 months post-operatively
MIRROR NCT03770559	2018	2024	MI-RAMPS *vs.* open RAMPS	Resectable PDAC body or tail	Post-operative LOS

CCI: Comprehensive complication index; DP: distal pancreatectomy; LOS: length of stay; MIDP: minimally invasive distal pancreatectomy; MI-RAMPS: minimally invasive radical antegrade modular pancreatosplenectomy; ODP: open distal pancreatectomy; OS: overall survival; PDAC: pancreatic ductal adenocarcinoma; RAMPS: radical antegrade modular pancreatosplenectomy; RFS: recurrence-free survival.

nodes retrieved, or resection margin status between the groups[74].

The LEOPARD 2 trial was published in 2019 and compared outcomes in minimally invasive PD *vs.* open approach in a multicenter, patient-blinded, and randomized controlled trial. This trial was separated into phase II and phase III, with the primary outcomes being safety and time to functional recovery, respectively. Fifty patients underwent a laparoscopic PD, whereas 49 patients underwent an open PD. The trial was prematurely terminated due to a difference in 90-day complication-related mortality (10% in laparoscopic *vs.* 0% in open) between the groups, although this was reported to not be statistically significant. Median time to functional recovery and pancreatic-specific and non-specific complication rates were comparable between the two groups[75]. Similar findings were seen in a 2023 meta-analysis by Yan *et al.*, who again showed no differences in serious complications (including pancreatic fistula, hemorrhage, and reoperation) or harvested lymph nodes but did note shorter LOS at the expense of increased operative times[76].

As shown above, although there have been benefits in short-term outcomes such as hospital LOS and no difference in oncologic or perioperative complications with minimally invasive approaches, there are disadvantages, including longer operative times for laparoscopic PD, similar to DP[77-80]. This was validated by 2020 and 2023 meta-analyses by Nickel *et al.* and Pfister *et al.*, respectively[81,82]. Dembinski *et al.* showed similar five-year overall and recurrence-free survival in patients undergoing laparoscopic PD *vs.* open PD. However, they did observe a higher need for re-interventions among patients who underwent the minimally invasive approach[83]. Vandeputte *et al.* performed a propensity score-matched comparison of the two techniques, which once again showed no difference in oncologic outcome. However, they did observe a higher complication rate for the minimally invasive approach[84]. Laparoscopic PD was associated with increased rates of pneumonia and abdominal infections in a retrospective review[85]. Taken together, further prospective randomized trials are needed to address these conflicting data.

The advent of the robot has rapidly expanded the utilization of a minimally invasive approach for PD. This may be due to the increased range of motion and dexterity of the robot to allow for easier reconstruction and, thus, a more achievable learning curve. A 2022 propensity score-match study published in the Journal of the American College of Surgeons showed longer operative times but less blood loss, LOS, and 30-day readmission for patients undergoing robotic PD compared to open PD[86]. van Oosten *et al.* found similar findings in their cohort of robotic PD at John's Hopkins[87]. Other studies have shown fewer complications and comparable oncologic outcomes for robotic PD compared to open, including a 2022 multi-institutional study from Zheng *et al*. looking at over 1,000 patients undergoing open *vs*. minimally invasive pancreas surgery for PNET[88-94]. These studies reveal that a robotic approach to PD is safe and feasible and allows a larger pool of surgeons to perform a minimally invasive PD as compared to a laparoscopic approach.

Future trials on minimally invasive pancreaticoduodenectomy

There are multiple ongoing clinical trials examining minimally invasive PD, as shown in Table 2. The PORTAL trial is a multicenter phase III patient-blinded trial with the primary outcome of time to functional recovery in patients with benign or malignant head of pancreas disease among patients undergoing open *vs*. robot-assisted PD. Secondary outcomes include overall complication rates, mortality, oncologic outcomes, cost, and quality of life. Patient recruitment is expected to be complete in 2022, with published results in 2024[95].

The TJDBPS01 trial (NCT03138213) is a multicentre, prospective, and randomized controlled trial that compares total laparoscopic PD to open PD. The authors hypothesize that laparoscopic PD has equal or better safety and post-operative recovery compared to an open approach with a primary outcome of hospital LOS[96]. Similarly, the TJDBPS07 trial (NCT03785743) is another ongoing randomized controlled trial, which will assess five-year overall and disease-free survival, 90-day mortality, and complication rates between laparoscopic and open PD[97]. Lastly, an ongoing trial from Johns Hopkins University (NCT04171440) is a randomized trial comparing minimally invasive PD to open PD. Patients with both benign and malignant pathologies are included with a primary outcome of time to functional recovery. Recruitment is currently ongoing, with results expected in 2024[68].

DISCUSSION

Based on a comprehensive review of prospective randomized trials, minimally invasive pancreatectomy is safe and has equivalent oncologic outcomes and morbidity compared to traditional open approaches when in experienced hands. The traditional open PD is a complex operation with numerous steps, requiring a mastery of abdominal anatomy and its variations and demanding technical excellence from the surgeon. The main limitations for minimally invasive pancreatectomy are the cost and increased operative times associated with the procedure. Additionally, the hesitation for universal adoption of minimally invasive pancreatectomy remains due to its associated learning curve required to achieve equivalent and optimal outcomes.

High intraoperative cost has been one of the main limitations to the adoption of minimally invasive surgery, specifically, the robotic approach. Much of the cost is related to increased operating room time and the cost of disposables and equipment used[98]. However, the benefits of minimally invasive approaches compared to open ones in terms of decreased LOS may counteract these costs[98]. A propensity score-matched analysis comparing robotic pancreatic surgery to open surgery showed a higher intraoperative cost with the robot; however, it also demonstrated a decreased overall hospital LOS, which improved overall cost-effectiveness[99]. Nevertheless, much of the literature evaluating cost is retrospective in nature, and prospective data is limited to single-center studies. Consequently, there is a need for multicenter prospective trials assessing the cost-effectiveness of minimally invasive approaches to pancreatic surgery.

The "learning curve" for surgeons is a well-known phenomenon with an inverse relationship between surgeon volume and mortality[100]. Much has been studied on the learning curve associated with minimally invasive pancreas surgery. A systematic review by Chan *et al*. analyzed the number of cases needed to surmount the learning curve and showed no difference in laparoscopic *vs*. robotic PD (34.1 cases *vs*. 36.7 cases, respectively)[101]. Another cohort study showed that the learning curve for proficiency was around

Table 2. Ongoing clinical comparing minimally invasive and open pancreaticoduodenectomy

Trial name	Year registered	Anticipated completion date	Groups	Patient population	Primary end point
NCT04211948	2019	2024	Robotic PD *vs.* OPD	PDAC	1 and 3-year OS
MIOP-NCT03747588	2018	2028	MIPD *vs.* OPD	Resectable PDAC, bile duct, ampullary cancer	30-day complications
PORTAL NCT04400357	2020	2022	Robotic PD *vs.* OPD	Resectable PDAC, periampullary cancer	Time to functional recovery
NCT04171440	2020	2024	Robotic PD	Benign + malignant pancreas or periampullary lesion	Hospital LOS
NCT03785743	2019	2027	Laparoscopic PD *vs.* OPD	PDAC	5-year OS
NCT03138213	2018	2022	Laparoscopic PD *vs.* OPD	Periampullary cancer	LOS
DIPLOMA-2 ISRCTN27483786	2022	2026	Robotic or laparoscopic PD *vs.* OPD	Premalignant or malignant disease	Safety and time to functional recovery

LOS: Length of stay; MIPD: minimally invasive pancreaticoduodenectomy; OPD: open pancreaticoduodenectomy; OS: overall survival; PD: pancreaticoduodenectomy; PDAC: pancreatic ductal adenocarcinoma.

20-25 cases, whereas a separate study showed improved operative times and performance in 30 cases[102,103]. One study found the number of cases needed to achieve proficiency in robotic PD was 40[104]. While the "exact" number of cases needed to achieve proficiency is heavily dependent on a number of factors (surgeon training, surgeon experience, operating room staff, *etc.*), intensive training programs focused on minimally invasive techniques are crucial to overcome this learning curve[105-107].

The extensive learning curve in minimally invasive pancreas surgery is due in part to the complexity of the reconstruction. Methods of reconstruction and management of the pancreatic stump during minimally invasive PD and DP, respectively, are crucial to reducing post-operative complications. Complications of minimally invasive pancreas surgery are similar to those encountered in open approaches, namely pancreatic leak or fistula, postpancreatectomy hemorrhage, anastomotic leak, bile leak, delayed gastric emptying, and pancreatogenic diabetes. Yet, as discussed in the sections above, there is no convincing data showing increased rates of complications or the need for further procedures to treat complications due to a minimally invasive approach.

The actual approach for minimally invasive pancreatectomy can be executed in several ways, including total laparoscopic or robotic alone, a hybrid approach where the robot is docked but in conjunction with a bedside assistant using laparoscopic instruments, or a hand-assisted approach. The superiority of these different techniques remains debatable and should depend on surgeon comfort and experience and various patient factors such as body mass, pancreatic duct size, and firmness of the gland. As such, there has been no definitive evidence to indicate a difference in pancreatic leak rate between any of these approaches[108,109]. Minimally invasive DP has similar morbidity compared to open approaches, with the advantages of quicker return to functional baseline, shorter hospital stay, and improved cosmetics. However, given the complexity of reconstruction, the advantages of minimally invasive PD are fewer. Nevertheless, as the robotic platform becomes more universally adopted and more commonly used, the technical acumen of surgeons to perform this complex surgery will increase, potentially leading to improved outcomes in the future for carefully selected patients.

Patient selection is important in choosing appropriate candidates for minimally invasive pancreas surgery. As is the case with all laparoscopic techniques, relative contraindications include a history of prior open surgery with abundant adhesive disease, which may preclude safe entry into the abdomen, and intolerance to pneumoperitoneum. Specific to pancreatic disease, pancreatitis or other forms of inflammation may distort planes and make dissection laparoscopically or robotically very challenging. Additionally, vascular involvement of tumors in borderline resectable or locally advanced disease may necessitate vascular reconstruction, which requires additional expertise to perform in a minimally invasive fashion. As a result, benign or low-grade malignant lesions without vascular lesions, such as neuroendocrine tumors, cystic lesions, and tumors of the ampulla of Vater, are best suited to minimally invasive PD[110,111]. A final consideration in appropriate candidates for minimally invasive pancreas surgery is body habitus. While obesity or thinness is not a contraindication, it presents unique challenges. In obese patients, the extra- and intra-abdominal adipose tissue can make finding appropriate planes challenging, whereas extremely thin patients may preclude adequate spacing of trocars to allow for a full range of motion.

While attempting to assess the most up-to-date, level 1 data regarding minimally invasive pancreatectomy, there are some limitations to the studies discussed above. Firstly, there may be inherent selection biases in some of the studies. Patients undergoing laparoscopic or robotic pancreatectomy would likely have differences in tumor size, malignant features, and vessel involvement, which could lead to more extensive surgery such as portal vein reconstruction. Additionally, patients with a more extensive history of abdominal surgery may not be ideal candidates for minimally invasive approaches.

While this review focused exclusively on minimally invasive PD and DP, there are current studies showing promising outcomes for minimally invasive central and total pancreatectomy as well, which will be an area of future research[112,113].

CONCLUSION

Overall, minimally invasive pancreatic resection remains a complex and technically challenging procedure that has seen significant improvement in morbidity and mortality over time and has been shown to be safe and efficacious in certain well-selected patient populations compared to open approaches. As the advent of minimally invasive approaches has been increasingly utilized for other abdominal or thoracic operations, laparoscopic and robotic techniques are slowly being adopted for pancreatic surgery. Several retrospective and a limited number of prospective studies support the use of minimally invasive pancreatic surgery in experienced centers. These benefits include a faster time to recovery, reduced pain, and shorter length of hospital stay following surgery. However, it is important to note that there are disadvantages, such as increased operative time and cost. Despite these promising results, additional data on long-term oncologic outcomes and survival are still needed for patients undergoing both PD and DP for cancer. Future planned and ongoing randomized studies will provide additional clarification regarding the safety and efficacy of minimally invasive pancreatic surgery.

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Authors' contributions

Made substantial contributions to the conception and writing of the manuscript: Shannon A, Bath NM, Ejaz A

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