



A COMPARISON OF MINIMALLY INVASIVE VS OPEN DISTAL PANCREATECTOMY FOR RESECTABLE PANCREATIC DUCTAL ADENOCARCINOMA

Ahmed Tabaan Alenezi*

Abstract

Background: Finding an effective treatment for PDAC has been a difficulty. Since surgical resection for PDAC is characterized by a high rate of morbidity and subsequent recurrence, a multimodal approach to PDAC management is recommended to improve both the expectancy and quality of life.

Objective: The present study aims to summarize current evidences comparing perioperative and oncological outcomes between MIPD and OPD for PDAC.

Methods: The current study is a systematic review article. Data were collected between 1 December 2021 and 30 February 2022. Medline and PubMed public database searches will be carried out for papers written all over the world on comparing MIPD and OPD for PDAC. The keyword search headings included "Minimally Invasive, Open, Distal, Pancreatectomy, Resectable Pancreatic Ductal Adenocarcinoma", and a combination of these were used. For additional supporting data, the sources list of each research was searched.

Results: PDAC accounts for high percentage of cancer-related mortality. It shows resistant to chemotherapy which necessitates surgical intervention. Minimally invasive distal pancreatectomy (MIDP) and Open Distal Pancreatectomy are the two main surgical interventions in the management of PDAC. Many researches reported the shift to MIDP due to many reasons such as less operative time and hospital stay time and less bleeding incidence. On the other hand ODP reported higher tumor size and high incidence of vessel resection. All the previously mentioned results indicate that MIDP is a promising management technique with more advantages than ODP.

Conclusion: MIDP is a promising management technique with more advantages than ODP.

Keywords: Minimally Invasive, Open, Distal, Pancreatectomy, Resectable Pancreatic Ductal Adenocarcinoma.

*Consultant of General Surgery & Administrator of North Medical Tower, Arar, Northern Saudi Arabia

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Introduction:

Pancreatic ductal adenocarcinoma (PDAC), which accounts for 90% of pancreatic cancers, is the world's fourth leading cause of cancer-related deaths. PDAC is one of the most chemoresistant cancers due to the wide heterogeneity of genetic mutations and the dense stromal environment [1]. Despite advances in pancreatic cancer research, the mortality to incidence ratio has not changed significantly over the last few decades. The five-year survival rate is still around 5–7%, and one-year survival is achieved in less than 20% of cases [2]. This bleak prognosis is largely due to a lack of visible and distinguishing symptoms, as well as reliable biomarkers for early diagnosis, as well as aggressive metastatic spread, which leads to poor response to treatments. In fact, approximately half of all diagnosed patients have metastatic disease [3].

Only 20-25 percent of all diagnosed pancreatic adenocarcinomas are distal pancreatic adenocarcinomas of the body or tail of the pancreas. While more proximal periampullary tumours usually present with jaundice, malabsorption, and pancreatitis, distal tumours usually present with vague symptoms such as weight loss and abdominal pain; as a result, distal cancers present at later stages than proximal cancers and are more likely to be metastatic or locally unresectable at the time of diagnosis [4, 5].

In many centres around the world, minimally invasive distal pancreatectomy (MIDP), first described by Gagner in 1996, is considered the standard approach for symptomatic benign and premalignant distal pancreas disease [6, 7]. Despite the fact that the number of pancreatic resections performed using a minimally invasive approach has increased significantly over the last two decades, the initial adoption of minimally invasive pancreatic surgery has been slow [8, 9]. In recent years, the feasibility and safety of minimally invasive distal pancreatectomy (MIDP) for benign pancreatic disease with postoperative outcome advantages have been reported [10]. However, because of the possibility of vessel resection, operation complexity, and oncological clearances, left-sided pancreatic ductal adenocarcinoma (PDAC) is only used in a limited number of cases. Despite the increased use of MIDP, reports indicate that laparoscopic distal pancreatectomy (LDP) has been performed on 3.9 percent -21 percent of the body or tail of a PDAC [11]. Three propensity score matching (PSM) analyses of MIDP for PDAC found not only comparable oncologic outcomes and advantages

of hospital stay, but also differences in the ratio of R0 resections, lymph node retrieval, small number of cases, and unclear indications [12]. Because of the complexity of vessel resections, this procedure should be used with resectable PDAC to broaden the indications for MIDP. MIDP's oncological safety is still being debated, which is impeding its further implementation [13].

Patients who are eligible for resection (resectable, borderline resectable) have the following surgical options: pancreaticoduodenectomy (head/body of pancreas and nearby organs are removed), distal pancreatectomy (tail, body, and spleen), total pancreatectomy (whole pancreas and nearby organs), or palliative surgery (stent or bypass), which may relieve symptoms of biliary and gastric outlet obstruction [14, 15]. Pancreaticoduodenectomy, first described by Whipple and Kausch at the turn of the twentieth century [16], is a three-step procedure that involves exploration, resection, and reconstruction. It is currently a risk-free procedure with low mortality and morbidity. Total pancreatectomy, which is reserved for a few indications, has been shown to have significantly worse postoperative recovery and outcome, primarily due to metabolic imbalance [17]. The scope of the resection has been widely debated in recent years; however, none of the procedures demonstrated a significant advantage over standard pancreaticoduodenectomy. Despite the low percentage of patients who undergo surgery, the chance of survival for surgical patients has increased significantly in the last few decades. Despite significantly higher postoperative complications, mortality rates do not exceed 5% [18]. The efficiency of surgery and the long-term survival of patients are determined in part by lymph-node infiltration, but also by the surgeon's expertise and the number of operations performed by the hospital. Sadly, even after successful resection, the median survival time is 20 months, with a 25% five-year survival rate [19]. The majority of resected patients (40%) experience tumour recurrence within 6–24 months of surgery, highlighting the importance of preoperative/postoperative therapies in order to achieve more effective treatments [20].

Study Rationale:

Since the introduction of minimally invasive distal pancreatectomy (MIDP) the implementation of this technique has been slow. The slow implementation rate could be related to the challenging nature of MIDP and uncertainty about

the clinical benefits as compared to open distal pancreatectomy (ODP). Few studies have compared perioperative and oncological outcomes between minimally invasive pancreatoduodenectomy (MIPD) and open pancreatoduodenectomy (OPD) for pancreatic ductal adenocarcinoma.

Study Objective:

The present study aims to summarize current evidences comparing perioperative and oncological outcomes between MIPD and OPD for PDAC.

Methodology:

Study Design: Review article.

Study duration Data were collected between 1 December 2021 and 30 February 2022.

Data collection Medline and PubMed public database searches will be carried out for papers written all over the world on comparing MIPD and OPD for PDAC. The keyword search headings included “Minimally Invasive, Open, Distal, Pancreatectomy, Resectable Pancreatic Ductal Adenocarcinoma”, and a combination of these were used. For additional supporting data, the sources list of each research will be searched. Criteria of inclusion: the papers will be chosen based on the project importance, English language, and 20 years’ time limit. Criteria for

exclusion: all other publications that do not have their main purpose in any of these areas or multiple studies and reviews will be excluded.

Statistical Analysis:

No predictive analytics technology will be used. To evaluate the initial results, the group members reviewed the data. The validity and minimization of error will be double revised for each member's results.

Results:

Table 1 illustrates the characters, methodology, outcomes of the included studies. It is clear from the table that DAC accounts for high percentage of cancer-related mortality.it shows resistant to chemotherapy which necessities surgical intervention. minimally invasive distal pancreatectomy (MIDP) and Open Distal Pancreatectomy are the two main surgical interventions in the management of PDAC. Many researched reported the shift to MIDP due to many reasons such as less operative time and hospital stay time and less bleeding incidence. On the other hand ODP reported higher tumor size and high incidence of vessel resection. All the previously mentioned results indicates that MIDP is a promising management technique with more advantages than ODP.

Table 1: Characters, methodology, outcomes of the included studies (n=5).

Author, year	Study type	Method	Outcomes
de Rooij T, van Hilst J, van Santvoort H, et al. (2019) [21]	multicenter patient-blinded randomized controlled superiority trial	Between April 2015 and March 2017, a multicenter patient-blinded randomised controlled superiority trial was conducted in 14 locations. Adult patients with pancreatic tumours on the left side that were limited to the pancreas and had no vascular involvement were randomly treated (1:1) to MIDP or ODP. The type of surgery was concealed from the patients by a thick abdominal bandage. The time to functional recovery was the key goal. The goal of the analysis was to find a way to help people.	Following MIDP, the time to functional recovery was 4 days for 51 patients against 6 days for 57 patients after ODP. The amount of blood lost during surgery was lower following MIDP, although the surgical time was greater. After MIDP, delayed gastric emptying grade B/C was detected less frequently. After MIDP, 39 percent of patients had grade B/C pancreatic fistulas, compared to 23 percent after ODP, with no change in percutaneous catheter drainage . When compared to ODP, the quality of life after MIDP was better, and overall costs were non-significantly lower. Following MIDP,

			there was no 90-day mortality compared to 2% after ODP.
van Hilst J, de Rooij T, Klompmaker et al (2019) [22]	pan-European propensity score matched (PSM) study	Between January 1st, 2007 and July 1st, 2015, all consecutive patients having a histological diagnosis of PDAC who underwent distal pancreatectomy (minimally invasive or open) with a histopathological diagnosis of PDAC were eligible for inclusion. Patients were excluded if they had had a previous pancreatic resection, had distant metastasis, had a tumour that affected the celiac trunc, or had a tumour that only became resectable following neo-adjuvant therapy. Patients were divided into two groups based on how they were operated on: MIDP or ODP. 1212 patients were included from 34 centers in 11 countries	MIDP indicated short-term clinical benefits, notably in terms of less intraoperative blood loss and a shorter hospital stay after surgery. Overall survival was comparable following both surgeries, however the oncological safety of MIDP for PDAC remains unknown because the R0 resection rate was higher in MIDP, while Gerota's fascia was resected less frequently and lymph node retrieval was lower. In PDAC, no significant differences in overall survival were found between MIDP and ODP, with overall survival ranging from 14 to 16 months.
Magge D, Gooding W, Choudry H, et al. (2013) [23]	Retrospective analysis	From March 1, 2002, to November 30, 2010, sixty-two patients were evaluated following surgical resection for distal PDC. medical oncology records, demographics, imaging, surgical summaries, anaesthetic logs, pathology reports, discharge summaries, and demographics were all assessed for patients . suspected borderline resectable or locally advanced disease were excluded from the sample. applying a propensity score is a predicted likelihood that a patient was chosen for ODP or MIDP based on a logistic regression model, this score aims to decrease bias and improve randomization . CCI and year of surgery were significantly associated with the propensity to perform MIDP	A total of 62 patients in this study, including 34 ODP (55%) and 28 MIDP (45%). Patients surviving at the end of the trial had a median observation duration of 25 months across the entire study. At a median follow-up of thirty months in the ODP group, eight patients were surviving, whereas at a median follow-up of 21 months in the MIDP group, 17 patients were alive, suggesting MIDP's recent adoption. High rates of margin-negative resection (ODP, 88 percent; MIDP, 86 percent) and median lymph node clearance (ODP, 12; MIDP, 11) were obtained in the 2 groups, with postoperative complications (ODP, 50 percent; MIDP, 39 percent) and pancreatic fistula (ODP, 29 percent; MIDP, 21 percent) occurring at similar rates and severity.

			MIDP showed less blood loss and hospital stay.
Kwon J, Park SY, Park Y, et al. (2021) [24]	retrospective study	Between January 2010 and December 2017, a total of 1868 individuals had distal pancreatectomy. Patients with PDAC who underwent distal pancreatectomy were included in the study. The study covered both MIDP and ODP participants. Patients with benign lesions, those with other kinds of pancreatic cancer, and cases of whole pancreatectomy or central pancreatectomy for PDAC were also excluded. Based on this criteria only 557 patients were enrolled in the study. Some clinicopathological data were obtained such as age, sex, operative time and tumor size. Follow-up every 3 months for 2 years was done and any detected recurrence was reported.	Among 557 patients 296 patients underwent MIDP and 261 patients underwent ODP. The MIDP and ODP groups did not differ substantially in terms of ASA score, proportion of elevated CA19-9, proportion of elevated CEA, age, gender, or proportion of mGPS. Operative time and length of hospital stay were shorter in MIDP than ODP. Clinical tumor size was smaller in MIDP group than that in the ODP group. Concurrent vessel resection was higher in ODP than MIDP. Overall surgical complications were not different between the MIDP and ODP groups
Chen, K., Pan, Y., Huang, Cj. et al. (2021) [25]	propensity score matching analyses	data of patients who underwent distal pancreatectomy (DP) and pancreaticoduodenectomy (PD) for PDAC between January 2004 and February 2020 were collected and used in this study. Diagnosis of PDAC was done using MRI or abdominal computed tomography. Patients in the DP group were split into two groups: LDP and ODP. A 1:1 propensity score matching (PSM) was performed via logistic regression analysis to reduce the effect of confounding factors and potential bias. The operating time, haemorrhage, transfusion, hospital stay, complications, adjuvant treatment, and time interval to adjuvant treatment were all assessed as perioperative outcomes.	In the DP group, there were no variations in comorbidity, previous abdominal surgery, or preoperative blood tests for cancer antigen 19-9 (CA19-9) and bilirubin between the LDP and ODP subgroups. Preoperative median bilirubin levels and preoperative median CA 19-9 levels were similar in the LDP and ODP subgroups. The LDP group had a significantly shorter mean operational time and a significantly lower median blood loss than the ODP group. There were fewer red blood cell transfusions necessary. Those in the LDP group versus those in the ODP group. Post-operative hospital stay was shorter for LDP than ODP.

<p>Björnsson, B et al(2020)[26]</p>	<p>randomized controlled trial</p>	<p>In an unblinded, parallel-group, single-centre superiority trial, consecutive patients evaluated at a multidisciplinary tumour board and scheduled for standard distal pancreatectomy were randomised prospectively to LDP or ODP. The primary outcome was the length of stay in the hospital after surgery.</p>	<p>Of the 105 patients who were screened, 60 were randomised and 58 were included in the study . the LDP group had 29 patients with an average age of 68 years and the ODP group had 29 patients with an average age of 63 years. Cystic pancreatic lesions were the most common reason, followed by neuroendocrine tumours. The median postoperative hospital stay in the laparoscopic group was 5 days compared to 6 days in the open group. After a median of 4 versus 6 days, functional recovery was achieved in both groups, and operation time was 120 minutes in both. Laparoscopic surgery resulted in less blood loss, with a median of 50 mL compared to 100 mL in the open group. There was no change in the complication rates. The rate of delayed stomach emptying was almost the same.in conclusion LDP is associated with shorter hospital stay than ODP, with shorter time to functional recovery and less bleeding</p>
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Discussion:

PDAC is one of the world's top causes of death. In the disciplines of medicine and surgery, finding an effective treatment for PDAC has been a difficulty. Since surgical resection for PDAC is characterized by a high rate of morbidity and subsequent recurrence, a multimodal approach to PDAC management is recommended to improve both the expectancy and quality of life. In several investigations, MIDP was found to have superior surgical results than ODP for PDAC[26-28]. While the indications of MIDP remains limited. After propensity score correction, Shin et al.[9] found that LDP was safer and more effective than ODP; however, the tumor size was smaller in LPD patients than in ODP patients. In a pan-European propensity-score-matched

investigation, the LDP and ODP groups had differing tumor locations, involvement of other organs, and the proportion of neoadjuvant treatment. Before PSM, the MIDP and ODP groups had varied neoadjuvant, tumor location, concurrent vascular resection, and concurrent resection of other organs, similar to prior publications.[29,30] Up until 2017, the number of MIDP trials increased, whereas the number of ODP trials decreased. Perioperative care, such as complication management, adjuvant chemotherapy, and radiation therapy, may improve during the research period. This improvement may have an impact on the finding that MIDP is linked to a higher chance of resectable PDAC survival. However, neither the

findings before nor after PSM revealed any differences in first-line adjuvant chemotherapy regimen between the groups. Furthermore, the prevalence of severe complications was low in all groups, and there was no statistically significant difference in severe complications between the groups, suggesting that perioperative therapy had no effect on survival rate in the current trial.[29]

According to some research, LDP operation time is equivalent to or longer than ODP operating time. Shorter operation times may be due to accumulated experience and standardized surgical techniques. The prolonged time spent doing ODP before PSM matching revealed that patients who received ODP had more severe PDAC than those who underwent MIDP. As a result, when the two groups were matched, there was no difference in operation times.[31,32] The MIDP group had much shorter postoperative hospital stays, and there were no differences in postoperative complications, or 90-day inpatient mortality rates between the MIDP and ODP groups. These findings have been replicated in a number of other research, demonstrating the viability of MIDP. The difference in postoperative hospital stays could be due to improved recovery in the MIDP group and is regarded an additional potential benefit of using the minimally invasive method, which is consistent with prior studies.[33,34]

MIDP is related with increased use of adjuvant chemotherapy, according to Anderson KL et al.[35], however the median time to start adjuvant chemotherapy was not different between the two groups. For left-sided PDAC, Raoof et al[36]. found no statistically significant differences in the proportion of adjuvant treatment and time to adjuvant chemotherapy initiation between LDP and ODP. Adjuvant treatment should be given earlier and completed for better patient outcomes, according to Kim HW et al.[37] MIDP could be useful in the treatment of PDAC because of its oncological benefits.

Conclusion:

MIDP is a promising management technique with more advantages than ODP.

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