Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/kx46xg79

LAPAROSCOPIC VERSUS OPEN PANCREATICODUODENECTOMY FOR PANCREATIC TUMORS: A COMPARISON OF OUTCOME PROFILES

Dr. Mohammad Zarin[1], Dr. Zia Ullah[1*], Dr. Muhammad Imran Khan[1], Dr. Shahzeb Khan[1], Dr. Izaz Ullah[2], Dr. Muhammad Ahmad[3], Dr. Samra Fakhar[1], Dr. Tayyab Afareen[1]

[1]Department of Surgery, Medical Teaching Institution, Khyber Teaching Hospital, Peshawar, Pakistan.
[2]Department of Surgery, Combined Military Hospital, Peshawar, Pakistan.
[3]Khyber Medical College, Peshawar, Pakistan.

***Corresponding Author:** Dr. Zia Ullah
*****Email: zia962015@gmail.com

ABSTRACT

Background: Pancreaticoduodenectomy (PD) is a complex surgical procedure primarily used to treat pancreatic and periampullary tumors, associated with high morbidity and mortality. The benefit and safety of laparoscopic pancreatoduodenectomy (LPD) for the treatment of pancreatic or periampullary tumors remain controversial.

Objective: To evaluate and compare the postoperative outcomes in patients undergoing laparoscopic versus open pancreaticoduodenectomy in a developing country.

Methods: This concurrent cohort study, conducted at Khyber Teaching Hospital, Peshawar, from September 2022 to September, 2024, enrolled 59 patients with resectable periampullary cancers. Data were collected using a specific proforma and analyzed with SPSS version 26. The independent t-test compared continuous variables between laparoscopic and open pancreaticoduodenectomy groups, the Chi-square test and logistic regression evaluated the impact of the procedures on outcomes.

Results: LPD was associated with a significantly shorter length of hospital stay (7.80days) compared to open PD (16.50days; $p<0.001$). Additionally, LPD resulted in significantly less blood loss (202.50ml) compared to OPD (415.00ml, $p<0.001$). The operative time for LPD was notably longer (357.00minutes) compared to OPD (230.00minutes; $p<0.001$). The rates of postoperative complications, including delayed gastric emptying, pancreatic fistula, and surgical site infections, were comparable between LPD and OPD, with no significant differences in overall morbidity and mortality ($p=0.506$).

Conclusion: LPD is a viable and effective procedure, offering benefits such as a shorter length of stay and reduced blood loss compared to OPD. However, the clinical advantages of LPD over OPD appear to be marginal, even with significant procedural expertise.

Keywords: Pancreaticoduodenectomy, Laparoscopy, Pancreatic Adenocarcinoma, Outcomes.

Introduction

Pancreatoduodenectomy (PD) is one of the most complicated abdominal surgeries and is considered the gold standard treatment for pancreatic and periampullary tumors [1]. Advances in imaging, surgical instrumentation, and enhanced surgical expertise have significantly improved the outcomes

of this complex procedure, with morbidity rates decreasing from 60% to 30% [1,2]. Despite these surgical advancements, pancreatic cancer remains the fourth leading cause of cancer-related deaths, with a 5-year survival rate of only about 12% [3]. The incidence of pancreatic cancer (PC) continues to rise, and it is projected to become the second most common cause of cancer-related mortality by 2030. Notably, pancreatic ductal adenocarcinoma (PDAC) is the most prevalent form of pancreatic cancer and ranks as the 14th most common cancer globally [4]. In the United States, PDAC is the fourth leading cause of cancer deaths, accounting for over 30,000 fatalities annually [5].

PD is the primary treatment for benign and resectable malignant tumors in the periampullary region or pancreatic head; however, it is associated with significant morbidity and mortality due to its complexity. The procedure was first popularized by Allen Oldfather Whipple, who published his initial case series in 1935, reporting a mortality rate of 25% [6]. Mortality remained high until the 1970s, and it was only in the 1990s that high-volume centers began consistently reporting mortality rates below 5% [7–9]. Today, with advancements in complication management, some Western centers report mortality rates as low as 2% [10], although complication rates remain high, ranging from 36-58% [11,12].

As surgical techniques advance, there is a growing trend toward minimally invasive approaches, including the shift from open to laparoscopic procedures. Laparoscopic pancreaticoduodenectomy (LPD) was first introduced by Gagner in 1994 and has since gained popularity as an alternative to the open approach, with approximately 746 laparoscopic procedures performed by 2016 [13,14]. Although LPD offers potential benefits such as reduced invasiveness, faster recovery, less postoperative pain, and enhanced visualization, surgeons require extensive training to achieve technical proficiency in this complex procedure [15]. A recent meta-analysis revealed that LPD, when performed by experienced surgeons in high-volume centers, yields non-inferior short-term surgical outcomes and oncologic adequacy compared to OPD, with additional benefits such as reduced overall morbidity, blood loss, and transfusion requirements, albeit with longer operative times [16].

In Pakistan, several centers perform PD, with mortality rates ranging from 3.1% to 13.9% [17,18]. However, there is limited data on LPD, which is increasingly becoming the global trend. Moreover, studies comparing the efficacy of LPD to OPD in developing countries are sparse. Therefore, this study aims to assess the efficacy of LPD versus OPD in Pakistan and to determine the outcome profiles of patients undergoing pancreaticoduodenectomy in a developing country.

Martial and Methods

This concurrent cohort study was conducted at Khyber Teaching Hospital, Peshawar, from September 2022 to September, 2024. The study included a sample of 59 patients, which is more than the calculated size of 55 using a 97% confidence interval and a 5% margin of error, based on a prevalence estimate of pancreatic cancer at 3% and population of 2,481,000 in Peshawar [19]. While the calculated minimum sample size was 30 patients, we included a total of 59 participants (30 in open pancreaticoduodenectomy while 29 in laparoscopic pancreaticoduodenectomy group) to enhance the study's statistical power and account for any potential loss of data due to incomplete follow-up. A non-probability convenience sampling strategy was employed to select participants.

Eligibility criteria included patients of either sex, aged 30 to 70 years, diagnosed with resectable periampullary cancers (such as distal cholangiocarcinoma, duodenal, ampullary, or pancreatic head cancer). Eligible patients were those with no radiological involvement of the superior mesenteric vein and portal vein and preserved fat planes between the tumor and critical vessels including the celiac axis, hepatic artery, and superior mesenteric artery. Only patients undergoing initial surgery without prior chemotherapy and those with no evidence of metastatic disease following staging laparoscopy were included. Exclusions were made for patients with unresectable disease identified at the outset or those whose disease was deemed irresectable based on intraoperative assessment. The study received approval from the Institutional Review Ethics Board (IREB) at Khyber Medical College.

Data collection was carried out using a specially designed proforma. Data analysis was performed using SPSS version 26. Quantitative variables were summarized as means with standard deviations, while qualitative variables were presented as frequencies and percentages. The independent t-test was

used to compare continuous variables, such as operative time, blood loss, and length of hospital stay, between Laparoscopic and open pancreaticoduodenectomy groups. The Chi-square test assessed associations between categorical variables, such as postoperative complications and surgical procedure types. Logistic regression analysis was conducted to evaluate the impact of the surgical procedure on various outcomes.

Results

The study included a total of 59 participants, with 29 patients undergoing laparoscopic pancreaticoduodenectomy and 30 undergoing open pancreaticoduodenectomy. The average age of the patients was 53.02 years, ranging from 33 to 68 years (±11.072), indicating a moderate variation in age distribution within the cohort, as shown in Table 1. The gender distribution was nearly equal, with 15 males (51.7%) and 14 females (48.3%) in the laparoscopic group, and 15 males (50.0%) and 15 females (50.0%) in the open procedure group.

The ASA Score distribution indicates that 55.0% of patients (n=33) were classified as ASA I, and 45.0% (n=27) as ASA II. The body mass index (BMI) of the patients ranged from 18 to 23, with a mean of 20.23 and a standard deviation of 1.423, suggesting that the patients were generally within a narrow BMI range. The tumor marker CA 19-9 levels ranged from 43 to 104 U/ml. The mean CA 19-9 level was 61.02 U/ml with a standard deviation of 16.738, showing moderate variability among the patients. The preoperative bilirubin levels were assessed in all 60 patients. The levels ranged from 1.0 to 22.0 mg/dL, with a mean value of 13.009 mg/dL ±4.8109 mg/dL.

Table 1. Descriptive statistics of the Demographic characteristics of the Participants

		Descriptive Statistics			
Variables	**Group**	**Minimum**	**Maximum**	**Mean**	**SD**
Age	LPD	38	65	52.2	8.628
	OPD	33	68	53.83	13.17
BMI	LPD	19	23	20.75	1.292
	OPD	18	22	19.72	1.378
CA-19.9 (U/mL)	LPD	45	104	69.04	19.42
	OPD	43	66	53	7.723
Pre-operation Bilirubin	LPD	1	22	13.18	5.412
	OPD	4	17	12.83	4.21
Pancreatic Duct Diameter	LPD	4	9	7.23	1.552
	OPD	5.6	9	7.55	1.098

Clinical Presentation of the Participants and Therapeutic Procedure

Symptoms distribution among laparoscopic pancreaticoduodenectomy (LPD) and open pancreaticoduodenectomy (OPD) groups is as follows: For the LPD group, fever was present in 21 patients (70.0%), jaundice in 27 patients (90.0%), epigastric pain with distention in 27 patients (90.0%), and anemia in 18 patients (60.0%). In the OPD group, fever was observed in 5 patients (16.7%), jaundice in 30 patients (100.0%), epigastric pain with distention in 30 patients (100.0%), and anemia in 15 patients (50.0%). Across both groups the overall analysis showed that fever was present in 26 patients (43.3%), jaundice in 57 patients (95.0%), epigastric pain with distention in 57 patients (95.0%), and anemia in 33 patients (55.0%). The results highlight the higher incidence of jaundice and epigastric pain with distention, particularly in the OPD group, while fever and anemia were more prevalent in the LPD group, as presented in Figure 1.

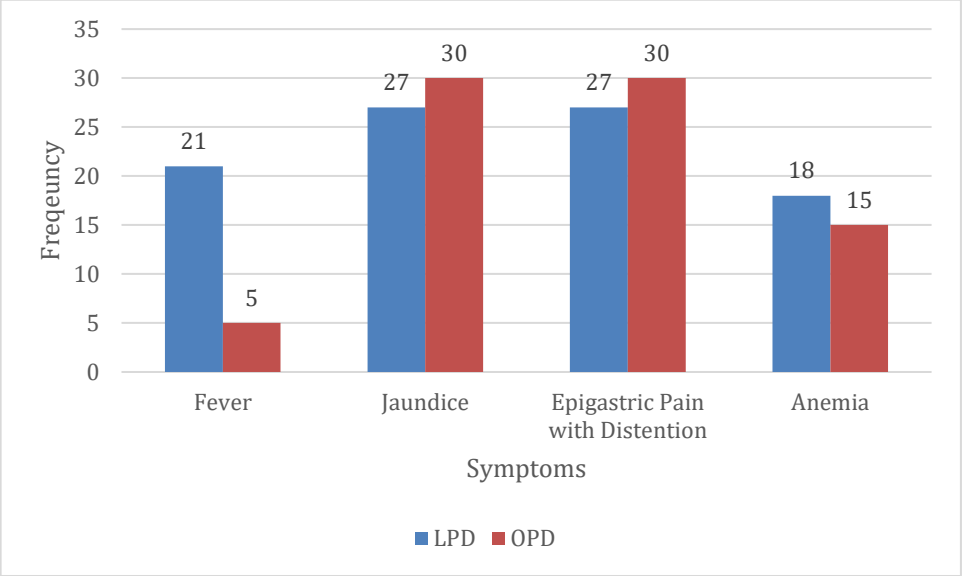

Figure 1. Clinical symptoms among the participants

Diabetes Mellitus (DM) was present in 15 patients in the LPD group (50.0%) and 15 patients in the OPD group (50.0%), totaling 30 patients (50.0%) across both groups. Hypertension was observed in 3 patients from the LPD group (10.0%) and 10 patients from the OPD group (33.3%), resulting in a total of 13 patients (21.7%) with hypertension across both groups, as shown in Figure 2.

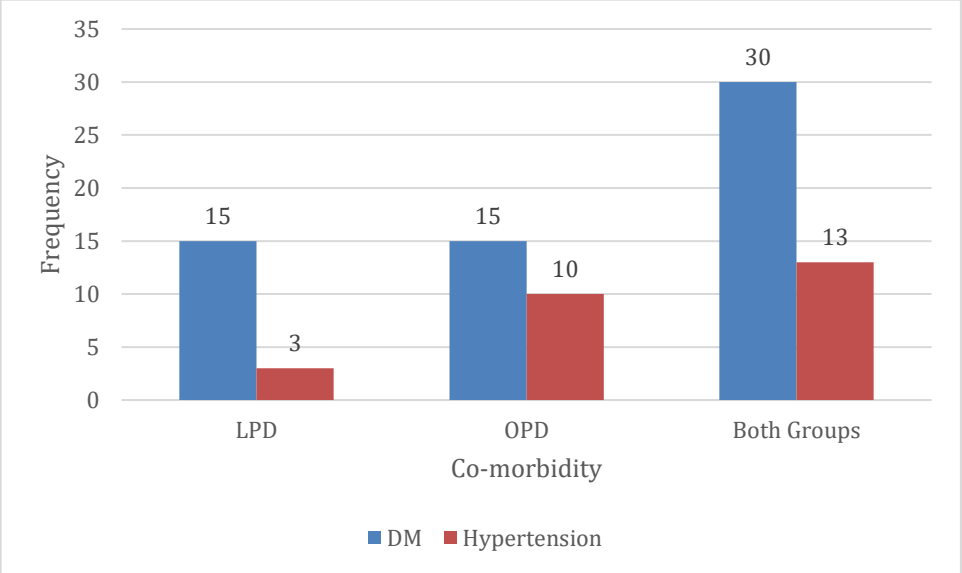

Figure 2. Co-morbidities among the participants

Comparative Analysis of LPD vs OPD Procedures

The duration of surgery varied widely, LPD had a mean duration of 357.00 minutes, with times ranging between 300 and 400 minutes ±31.856. In contrast, OPD had a shorter mean operative time of 230.00 minutes, ranging from 190 to 300 minutes ±36.199.

The blood loss ranged from 145 to 500 ml, with an average of 308.75 ml ±120.365 ml. For LPD patients, blood loss ranged from 145 to 260 ml, with a mean of 202.50 ml ±42.624 ml. Conversely, OPD patients experienced a significantly higher mean blood loss of 415.00 ml, with values ranging from 320 to 500 ml ±65.588 ml. These findings are illustrated in Table 2.

The overall mean length of hospital stay for all patients was 12.15 days, with a range from 5 to 22 days ±5.793 days, indicating moderate variability in the duration of hospital stays among the patients. Specifically, for patients who underwent laparoscopic pancreaticoduodenectomy (LPD), the mean length of hospital stay was significantly shorter at 7.80 days, ranging from 5 to 17 days ±3.605 days.

This suggests a relatively narrow range and less variability in hospital stay durations for the LPD group. In contrast, patients who underwent OPD had a longer average hospital stay of 16.50 days, with stays ranging from 10 to 22 days ±4.015 days.

The independent sample t-test analysis revealed that the mean length of hospital stay was significantly shorter for LPD compared to OPD, with a highly significant p-value of <0.001. Blood loss was also significantly lower in the LPD group compared to the OPD group, with a p-value of <0.001. Conversely, the duration of surgery was significantly longer for LPD than for OPD, also with a p-value of <0.001. These findings highlight significant procedural differences between LPD and OPD, with LPD resulting in less blood loss and shorter hospital stays but requiring longer operative times.

Table 2. Analysis of Operative time, Blood loss, and length of stay in both groups

Independent T-test for LPD & OPD groups					
	Minimum	Maximum	Mean	Std. Deviation	p-values
Operative time of LPD (minutes)	300	400	357.00	31.85	<0.001
Operative time of OPD (minutes)	190	300	230.00	36.19	
Blood loss in LPD	145	260	202.50	42.62	0.001
Blood Loss in OPD	320	500	415.00	65.58	
Length Of Hospital Stay (Days) of Laparoscopic PD	30	5	17	7.80	<0.001
Length Of Hospital Stay (Days) of Open PD	30	10	22	16.50	

Characteristics of Pancreatic Tumor

Tumor characteristics were assessed, revealing that the majority were diagnosed with adenocarcinoma (83%, n=49), while 17% (n=10) had neuroendocrine tumors. The distribution between the laparoscopic pancreaticoduodenectomy (LPD) and open pancreaticoduodenectomy (OPD) groups was relatively balanced, with 24 patients in the LPD group and 25 in the OPD group diagnosed with adenocarcinoma. The size of the tumors ranged from a minimum of 2.00 cm to a maximum of 9.00 cm. The mean tumor size was 5.06 cm ±2.28.

Regarding surgical margins, 30.5% (n=18) of patients had no clear margins, with 8 in the LPD group and 10 in the OPD group. In contrast, 69.5% (n=41) achieved clear margins, showing a relatively even distribution between the two groups (21 in LPD and 20 in OPD). The p-value of Chi-square test for the association between surgical approach and clear margins was 0.632, indicating no statistically significant difference between the groups in this regard, as shown in Table 3.

Table 3. Pancreatic Tumor Type and Characteristics

Variables		Percentage	LPD Group (n)	OPD Group (n=)	p-value
Type of Tumor	Neuroendocrine Tumor	17% (10)	5	5	
	Adenocarcinoma	83% (n=49)	24	25	
	Total	100% (n=59)	29	30	
	Total	100% (n=59)	29	30	
Clear Margins	No	30.5% (n=18)	8	10	0.632
	Yes	69.5% (n=41)	21	20	
	Total	100% (n=59)	29	30	

Correlation analysis of Outcomes in LPD vs OPD groups

For LPD, the majority of patients did not require a blood transfusion (Packed cell). Specifically, 10.0% of patients received no blood transfusion, 10.0% received 1 unit, and another 10.0% received 2 units. A larger portion of the LPD patients required more transfusions, with 20.0% receiving 3 units, 30.0% receiving 4 units, 10.0% receiving 5 units, and 10.0% receiving 7 units. In contrast, for OPD patients, the transfusion requirements were more concentrated: 33.3% of OPD patients received 5 units, another 33.3% received 6 units, and the remaining 33.3% received 7 units. No patients in the OPD group received fewer than 5 units of blood transfusion.

Crosstab analysis of outcomes in both groups was performed, and the Chi-square test was used to assess associations, as presented in Table 4. There were 22 cases of delayed gastric emptying, with 12 cases in the LPD group and 10 in the OPD group. The Chi-square test results show no significant association between the type of surgical procedure and delayed gastric emptying ($p = 0.592$).

Anastomotic disruptions were observed in the following categories:

1. **Pancreatojejunostomy leaks:** 1 case in the LPD group and 1 case in the OPD group.
2. **Gastrojejunostomy leaks:** 1 case in the LPD group, and no cases in the OPD group.
3. **Choledochojejunostomy leaks:** 1 case in the LPD group, and no cases in the OPD group.

The Chi-square test indicates a marginally significant association between the type of surgical procedure and the occurrence of anastomotic disruption ($p = 0.076$). Post-pancreatectomy hemorrhage occurred in 18 patients, with 3 cases in the LPD group and 15 cases in the OPD group. The Chi-square test reveals a significant association between the type of surgical procedure and post-pancreatectomy hemorrhage ($p = 0.001$). Post-operative collections were observed in 6 patients, all of whom had undergone LPD. The Chi-square test could not be computed for this variable, as it had only one category within the procedure type, and hence, no statistical analysis was performed.

Surgical site infections were identified in 29 patients, with 21 cases in the LPD group and 8 in the OPD group. The Chi-square test indicates a significant association between the type of surgical procedure and surgical site infections ($p < 0.001$). The Clavien-Dindo classification showed varied grades of complications, with the Chi-square test showing a significant difference in complication grades between LPD and OPD procedures ($p = 0.012$). Regarding post-operative outcomes, including improved condition, the mortality rate was 10% (n=3) for the LPD group and 12% (n=4) for the OPD group. However, there were no significant differences between the types of procedures and post-operative outcomes ($p = 0.506$).

Table 4. Outcomes analysis in LPD vs OPD groups

Variables		Surgical Procedure			
		LPD	OPD	Total	p-value
Delayed Gastric Emptying	Yes	12	10	22	0.592
	No	17	20	37	
	Total	29	30	59	
Anastomotic disruption	None	26	29	55	0.076
	Pancreatojejunostomy leaks	1	1	2	
	Gastrojejunostomy leaks	1	0	1	
	Choledochojejunostomy leaks	1	0	1	
	Total	29	29	58	
Post Pancreatectomy Haemorrhage	None	26	15	41	0.001
	Grade A	3	15	18	
	Total	29	30	59	

Surgical Site Infection	None	20	5	25	<0.001
	Superficial	9	20	29	
	Deep	0	5	5	
	Total	29	30	59	
Claiven-Dindo Grade	Grade I	18	10	28	0.012
	Grade II	3	10	13	
	Grade III	3	5	8	
	Grade IV	0	3	3	
	Total	24	28	52	
Mortality		3	4	7	0.506
	Total	29	30	59	

The multinomial logistic regression analysis was conducted to examine the association between the type of surgical procedure (LPD vs. OPD) and post-operative outcomes categorized as improved, mortality, and morbidity. The model did not significantly improve the prediction of outcomes with a chi-square value of 1.375, 2 degrees of freedom, and a p-value of 0.503. When comparing "improved" outcomes relative to "morbidity," the coefficient for LPD was 0.000, with a p-value of 1.000, showing no significant effect. Similarly, for "mortality" outcomes relative to "morbidity," the coefficient for LPD was -0.693, with a p-value of 0.384, which also indicates no significant effect. The analysis suggests that the type of surgical procedure does not have a statistically significant impact on the likelihood of different post-operative outcomes, as indicated by the non-significant p-values.

Discussion

The findings of our study provide valuable insights into the comparative outcomes of laparoscopic versus open pancreaticoduodenectomy. Despite advancements in minimally invasive techniques, our results indicate that the choice between LPD and OPD may not significantly influence certain post-operative outcomes, such as overall improvement, morbidity, or mortality. However, significant differences were observed in specific intraoperative and postoperative variables, highlighting the nuanced impact of surgical approach on patient recovery and complication rates.

Our study found significant differences LPD and OPD concerning operative time, blood loss, and length of hospital stay. The mean operative time for LPD was notably longer at 357 minutes compared to 230 minutes for OPD ($p < 0.001$). However, LPD resulted in significantly less blood loss, with a mean of 202.5 mL versus 415 mL in the OPD group ($p < 0.001$). Additionally, the length of hospital stay was significantly shorter for patients who underwent LPD, averaging 7.8 days compared to 16.5 days for those who underwent OPD ($p < 0.001$).

In contrast to the findings by Yin et al., reported no significant difference in the length of stay and complications between laparoscopic and open pancreaticoduodenectomy (OPD), our study observed significant differences in these areas [1]. Specifically, we found that patients who underwent LPD had a significantly shorter length of hospital stay compared to those who underwent OPD ($p <0.001$). Nickel et al. also reported longer operative times and minimal blood loss for LPD compared to OPD, these findings are consistent with our results [20]. Our findings are consistent with those reported by Min et al. Specifically, we also observed that the postoperative length of stay was significantly shorter for patients in the LPD group compared to the OPD group, with a mean difference favoring LPD (7.80 days vs. 16.50 days, $p < 0.001$). Additionally, while Yin et al. reported no significant differences in complications between the two procedures, our study identified significant associations between the type of procedure and various post-operative complications, such as post-pancreatectomy hemorrhage and surgical site infections, with LPD showing a lower incidence of severe complications in some cases [1]. Feng et al. found that LPD led to significantly better outcomes in several areas compared to OPD. Specifically, LPD was associated with a longer operative time, lower rates of severe

complications (Clavien-Dindo grade ≥III), less blood loss, and shorter hospital stays. These findings align with the results of our study, where LPD demonstrated a longer operative time, reduced blood loss, and shorter postoperative hospital stays compared to OPD [4].

Unlike Yin et al., who found no significant difference in these severe complications, our results showed that surgical site infections were significantly more common in the LPD group compared to the OPD group ($p < 0.001$). Moreover, the distribution of Clavien-Dindo grades differed significantly between the two procedures ($p = 0.012$), with higher grades of complications more prevalent in OPD patients [1]. Our results diverge slightly regarding the incidence of serious postoperative morbidities. While Min et al. reported no significant difference in the incidence of serious morbidities (Clavien-Dindo grade ≥ III) between the two groups, our study found a significant difference in the distribution of Clavien-Dindo grades, with higher grades more prevalent in OPD patients ($p = 0.012$) [21].

Alberto et al. reported that LPD significantly reduced hospital length-of-stay, estimated blood loss, infectious and pulmonary complications, overall complications, postoperative bleeding, and hospital readmission compared to OPD [22]. These findings are consistent with our results, which also showed that LPD was associated with reduced blood loss and a shorter hospital stay. However, our study did not find significant differences in overall complications or hospital readmission rates between LPD and OPD. Stauffer et al. reported that LPD had a significantly longer operative time compared to OPD. However, they found that LPD was associated with lower blood loss and a reduced transfusion rate. Postoperative complications, and the length of hospital stay was similar between the two procedures [5]. These findings align with our study, which also observed a longer operative time for LPD but highlighted its advantages in terms of reduced blood loss and transfusion requirements. The overall rates of postoperative complications and hospital stay did not differ significantly between LPD and OPD in our study. Our study revealed no significant difference in post-operative mortality between LPD and OPD procedures, with a p-value of 0.506. This contrasts with the findings of Yin et al., who reported higher mortality rates associated with LPD compared to OPD [1]. unlike Feng et al., our study did not find significant differences in the rate of severe complications or overall morbidity between the two groups who reported lower mortality rates in LPD [4].

This study has several limitations. The relatively small sample size, the retrospective nature of the study may introduce selection bias, and variations in surgical techniques or postoperative care across different institutions could impact outcomes. Recommendations for future research include conducting larger, multicenter randomized controlled trials to validate these findings and minimize biases. A more detailed analysis of long-term outcomes, including quality of life and recurrence rates, would provide a more comprehensive understanding of the advantages and limitations of laparoscopic versus open approaches.

Conclusion

These findings suggest that while laparoscopic PD may involve a longer surgical duration, it offers significant advantages such as reduced blood loss and quicker postoperative recovery compared to open pancreaticoduodenectomy (OPD). Although OPD has a shorter operative time, the overall benefits of LPD, including less blood loss and a shorter hospital stay, make it a favorable option for eligible patients. Nevertheless, careful patient selection and the surgeon's expertise are essential to minimize the likelihood of conversion to open surgery. Importantly, the rates of postoperative complications were similar between the two approaches, underscoring the need to carefully weigh the benefits and potential risks of each method.

References

1. Yin T, Qin T, Wei K, Shen M, Zhang Z, Wen J, Pan S, Guo X, Zhu F, Wang M, Zhang H, Hilal MA, Qin R. Comparison of safety and effectiveness between laparoscopic and open pancreatoduodenectomy: A systematic review and meta-analysis. International Journal of Surgery. 2022 Sep 1;105:106799.
2. Klompmaker S, Van Hilst J, Wellner UF, Busch OR, Coratti A, D'Hondt M, Dokmak S, Festen S, Kerem M, Khatkov I, Lips DJ, Lombardo C, Luyer M, Manzoni A, Molenaar IQ, Rosso E,

Saint-Marc O, Vansteenkiste F, Wittel UA, Bonsing B, Groot Koerkamp B, Abu Hilal M, Fuks D, Poves I, Keck T, Boggi U, Besselink MG. Outcomes after minimally-invasive versus open pancreatoduodenectomy: A pan-european propensity score matched study. Ann Surg [Internet]. 2020 Feb 1 [cited 2024 Aug 27];271(2):356–63. Available from: https://journals.lww.com/annalsofsurgery/fulltext/2020/02000/outcomes_after_minimally_invasive_versus_open.25.aspx

3. Pinchot SN, Weber SM. Pancreaticoduodenectomy. Illustrative Handbook of General Surgery: Second Edition [Internet]. 2020 Aug 19 [cited 2024 Aug 27];699–713. Available from: http://europepmc.org/books/NBK560747
4. Feng Q, Liao W, Xin Z, Jin H, Du J, Cai Y, Liao M, Yuan K, Zeng Y. Laparoscopic Pancreaticoduodenectomy Versus Conventional Open Approach for Patients With Pancreatic Duct Adenocarcinoma: An Up-to-Date Systematic Review and Meta-Analysis. Vol. 11, Frontiers in Oncology. Frontiers Media S.A.; 2021.
5. Stauffer JA, Coppola A, Villacreses D, Mody K, Johnson E, Li Z, Asbun HJ. Laparoscopic versus open pancreaticoduodenectomy for pancreatic adenocarcinoma: long-term results at a single institution. Surg Endosc. 2017 May 1;31(5):2233–41.
6. Torphy RJ, Fujiwara Y, Schulick RD. Pancreatic cancer treatment: better, but a long way to go. Surg Today. 2020;50(10):1117–25.
7. Simon R. Complications after pancreaticoduodenectomy. Surgical Clinics. 2021;101(5):865–74.
8. Hunger R, Seliger B, Ogino S, Mantke R. Mortality factors in pancreatic surgery: A systematic review. How important is the hospital volume? International Journal of Surgery. 2022;101:106640.
9. Cawich SO, Cabral R, Douglas J, Thomas DA, Mohammed FZ, Naraynsingh V, Pearce NW. Whipple's procedure for pancreatic cancer: training and the hospital environment are more important than volume alone. Surgery in Practice and Science. 2023;14:100211.
10. Del Valle JP, Mahvi DA, Fairweather M, Wang J, Clancy TE, Ashley SW, Urman RD, Whang EE, Gold JS. The improvement in post-operative mortality following pancreaticoduodenectomy between 2006 and 2016 is associated with an improvement in the ability to rescue patients after major morbidity, not in the rate of major morbidity. Hpb. 2021;23(3):434–43.
11. Smits FJ, Verweij ME, Daamen LA, van Werkhoven CH, Goense L, Besselink MG, Bonsing BA, Busch OR, van Dam RM, van Eijck CHJ. Impact of complications after pancreatoduodenectomy on mortality, organ failure, hospital stay, and readmission: analysis of a nationwide audit. Ann Surg. 2022;275(1):e222–8.
12. van Rijssen LB, Zwart MJ, Van Dieren S, de Rooij T, Bonsing BA, Bosscha K, van Dam RM, van Eijck CH, Gerhards MF, Gerritsen JJ. Variation in hospital mortality after pancreatoduodenectomy is related to failure to rescue rather than major complications: a nationwide audit. Hpb. 2018;20(8):759–67.
13. Kolbeinsson HM, Chandana S, Wright GP, Chung M. Pancreatic cancer: a review of current treatment and novel therapies. Journal of Investigative Surgery. 2023;36(1):2129884.
14. Yin T, Qin T, Wei K, Shen M, Zhang Z, Wen J, Pan S, Guo X, Zhu F, Wang M, Zhang H, Hilal MA, Qin R. Comparison of safety and effectiveness between laparoscopic and open pancreatoduodenectomy: A systematic review and meta-analysis. International Journal of Surgery [Internet]. 2022;105:106799. Available from: https://www.sciencedirect.com/science/article/pii/S1743919122005763
15. Feng Q, Xin Z, Zhu B, Liao M, Liao W, Zeng Y. Perioperative and short-term oncological outcomes following laparoscopic versus open pancreaticoduodenectomy after learning curve in the past 10 years: a systematic review and meta-analysis. Gland Surg. 2021;10(5):1655.
16. Yan Y, Hua Y, Chang C, Zhu X, Sha Y, Wang B. Laparoscopic versus open pancreaticoduodenectomy for pancreatic and periampullary tumor: a meta-analysis of randomized controlled trials and non-randomized comparative studies. Front Oncol. 2023;12:1093395.

17. Jamal A, Shakeel O, Mohsin J, Malik AA, Haq IU, Begum S, Khan SM, Hanif F, Kabir SI, Syed AA. Pancreaticoduodenectomy: Outcomes of a complex surgical procedure from a developing country. Pancreatology. 2020;20(7):1534–9.
18. Noor MA, Hanif F, Shakeel O, Bari H. Pancreaticogastrostomy: a safe option in pancreaticoduodenectomy for pancreatic head and periampullary neoplasms. Journal of the College of Physicians and Surgeons Pakistan. 2020;30(1):51–6.
19. Pancreatic cancer incidence statistics | Cancer Research UK. [cited 2024 Sep 25]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/pancreatic-cancer/incidence#heading-Zero
20. Nickel F, Haney C, Probst P, Kowalewski KF, Diener M, Limen E, Strobel O, Müller-Stich BP, Hackert T. Laparoscopic versus open pancreaticoduodenectomy a systematic review and meta-analysis of randomized controlled trials. HPB. 2020;22:S322.
21. Wang M, Li D, Chen R, Huang X, Li J, Liu Y, Liu J, Cheng W, Chen X, Zhao W, Li J, Tan Z, Huang H, Li D, Zhu F, Qin T, Ma J, Yu G, Zhou B, Zheng S, Tang Y, Han W, Meng L, Ke J, Feng F, Chen B, Yin X, Chen W, Ma H, Xu J, Liu Y, Lin R, Dong Y, Yu Y, Liu J, Zhang H, Qin R. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours: a multicentre, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol [Internet]. 2021 Jun 1 [cited 2024 Aug 27];6(6):438–47. Available from: http://www.thelancet.com/article/S2468125321000546/fulltext
22. Aiolfi A, Lombardo F, Bonitta G, Danelli P, Bona D. Systematic review and updated network meta-analysis comparing open, laparoscopic, and robotic pancreaticoduodenectomy. Vol. 73, Updates in Surgery. Springer Science and Business Media Deutschland GmbH; 2021. p. 909–22.