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ORIGINAL ARTICLE

Comparison of Long-Term Oncologic and Perioperative Outcomes of Minimally Invasive and Open Pancreatoduodenectomy for Resectable and Borderline Resectable Pancreatic Ductal Adenocarcinoma: Exploring Type 0 Resection as a Potential Indication for MIPD

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ABSTRACT

Background: The safety and efficacy of minimally invasive pancreatoduodenectomy (MIPD) for pancreatic ductal adenocarcinoma (PDAC) remain controversial. This study evaluated the surgical and oncological outcomes of MIPD versus open pancreatoduodenectomy (OPD) after overcoming the MIPD learning curve.

Methods: Between April 2014 and July 2022, 357 patients underwent pancreatoduodenectomy for resectable (RPC) or borderline resectable (BRPC) PDAC. After excluding early-phase MIPD cases, 112 patients underwent MIPD and 245 underwent OPD. Propensity score matching was performed. Subgroup analysis assessed outcomes in patients undergoing PD without vascular resection (type 0).

Results: MIPD was associated with longer operation time ($p = 0.002$), but similar estimated blood loss and intraoperative transfusion volumes. Rates of clinically relevant postoperative fistula and delayed gastric emptying were comparable. Disease-free survival (DFS) and overall survival (OS) did not differ significantly between MIPD and OPD groups ($p = 0.670$ and $p = 0.179$, respectively). In type 0 resections, OS was equivalent, but DFS was significantly better in the MIPD group.

Conclusions: MIPD is a safe and feasible option for RPC and BRPC PDAC, with oncologic outcomes comparable to OPD. Type 0 tumors, not requiring vascular resection, may represent an optimal indication for MIPD.

1 | Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest cancers with poor overall survival (OS) rates. Despite the availability of various neoadjuvant and adjuvant treatment strategies, surgical resection remains the only potentially curative treatment option for PDAC. Recently, minimally invasive pancreatoduodenectomy (MIPD) has been developed and proven effective for periampullary tumors. Studies have demonstrated that MIPD is safe, viable, and offers favorable perioperative outcomes, including reduced blood loss, fewer transfusions, and shorter hospital stays compared to traditional open pancreatoduodenectomy (OPD) [1–3].

The effectiveness of MIPD for PDAC remains debated, unlike its use for periampullary tumors [4]. Challenges, such as the intricate

dissection near the superior mesenteric artery, the need for thorough lymph node harvesting, and frequent tumor involvement in vascular structures, complicate the adoption of MIPD for PDAC. Despite these challenges, various studies suggest that MIPD can provide equivalent or superior perioperative outcomes, maintain comparable long-term survival rates, and is technically feasible and oncologically safe for treating PDAC [5, 6].

Currently, evidence supporting the management of PDAC with MIPD is insufficient, and the optimal indications for the use of MIPD in PDAC have not yet been established. Therefore, this study performed a retrospective analysis to compare the perioperative and long-term oncological outcomes of MIPD with those of OPD in patients with resectable (RPC) and borderline resectable (BRPC) PDAC using propensity score matching. This study aimed to identify the most suitable indications for MIPD in these patients.

2 | Methods

2.1 | Study Design and Data Collection

In this study conducted at a single center, 408 patients who underwent pancreatoduodenectomy (PD) for RPC and BRPC were initially enrolled. After excluding patients with locally advanced PDAC or distant metastasis, 359 patients were eligible for the final propensity score-matched analysis. To determine whether PD without vascular resection (type 0 resection) could be an optimal approach for MIPD in cases of RPC and BRPC, we further excluded patients who had undergone vascular and combined organ resection and conducted an additional analysis (Figure 1). Of these, 249 underwent OPD, 66 underwent laparoscopic PD (LPD), and 44 underwent robot-assisted LPD (RALPD). All MIPD procedures were performed after a learning curve based on a previous study [7]. The study was approved by the Institutional Review Board of Yonsei University College of Medicine (approval number 4-2024-0382).

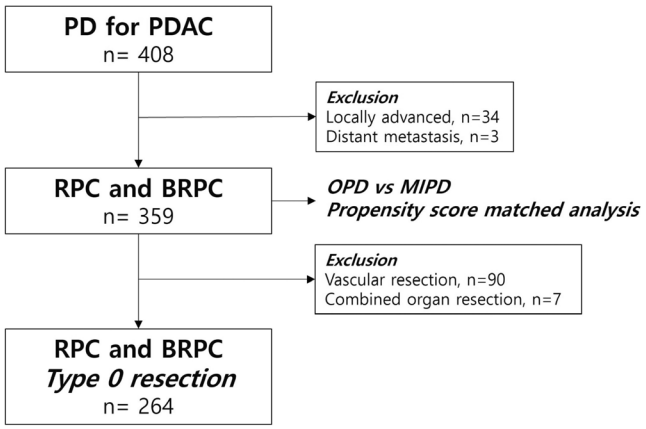

FIGURE 1 | Study flow diagram.

2.2 | Patient Variables and Definitions (Three Types of Surgical Extent of MIPD)

Data, including baseline demographics, perioperative details, and pathology outcomes, were retrospectively collected from the electronic medical records. We analyzed variables such as operation time, estimated blood loss (EBL), need for blood transfusions, and conversion to open surgery. Postoperative complications including postoperative pancreatic fistulas (POPF), delayed gastric emptying (DGE), and postoperative pancreatectomy hemorrhage (PPH). Additionally, the duration of postoperative hospital stay, tumor pathology (American Joint Committee on Cancer Stage [AJCC], 8th edition), reoperation rate, 90-day readmission, and 90-day mortality were evaluated. The resection margin status was categorized as R0 or R1. If the closest safe resection margin was <1 mm, it was categorized as R1 [8].

In this study, the scope of MIPD for pancreatic cancer was classified into different types based on surgical complexity, according to our previous definition [4]. Type 0 MIPD involves standard PD without vascular resection. Type I MIPD includes combined venous vascular resection, typically involving tangential (wedge) resection of the portal vein or superior mesenteric vein with primary repair and is categorized as Type Ia MIPD. Type Ib MIPD involves more complex surgical interventions to achieve margin-negative resections, such as tangential resections with patch repair, segmental resections with end-to-end anastomosis, or using artificial grafts for reconstruction. Type II MIPD, which involves combined arterial resections, is considered in selected cases but is relatively rare (Table 1).

2.3 | Surgical Methods

The techniques for port placement and the MIPD procedure were performed according to methods outlined in a previously published report [9–11]. During the reconstruction phase, end-to-side pancreaticojejunostomies, end-to-side hepaticojejunostomies,

TABLE 1 | Three types of surgical extent of MIPD.

Type 0	Type Ia	Type Ib	Type II
Standard lymphadenectomy			
Not require vascular resection	Combined VENOUS vascular resection		Combined ARTERIAL resection
	Tangential (wedge) resection of PV or SMV with primary repair	Tangential resection with patch repair, segmental resection with end-to-end anastomosis or reconstruction	

and side-to-side duodenojejunostomies were performed. RALPD followed the same steps as the LPD up to the resection phase. However, the reconstruction phase for RALPD was executed using a robotic system. At our center, standard dissection is generally performed for pancreatic cancer. Periarterial divestment was occasionally required in BRPC cases that ultimately underwent type 0 resection after neoadjuvant therapy. However, objective data on the exact frequency or extent of periarterial divestment were not available.

2.4 | Statistical Analysis

Statistical analyses were conducted using SPSS software (version 25.0; SPSS Inc., Chicago, IL, USA). Continuous variables are presented as means ± standard deviation, whereas categorical variables are expressed as percentages or frequencies. To compare continuous variables, either the Mann–Whitney *U* test or Student's *t*-test was used. Categorical data were compared using Fisher's exact test or the chi-square test. Logistic regression analysis was used to identify the predictive factors for clinically relevant (CR)-POPF. Statistical significance was set at $p < 0.05$.

2.5 | Propensity Score Matching

Propensity score matching (PSM) analysis was performed to minimize bias from potential confounders. Propensity scores were generated using binary logistic regression, and patients with closely matched scores were paired in a 1:1 ratio using a nearest-neighbor algorithm with a caliper width of 0.2 of the standard deviation of the logit of the propensity score. The matching model included covariates such as age, ASA physical status, body mass index (BMI), clinical T and N stage, tumor size, CA19-9, resectability status, and receipt of neoadjuvant therapy. Postmatching balance was confirmed, as shown in Table S1, where previously imbalanced variables (e.g., age, ASA class, CA19-9, and resectability status) demonstrated no significant differences between the MIPD and OPD groups (all $p > 0.1$).

3 | Results

3.1 | General Characteristics of Patients

The MIPD group had a higher proportion of older patients ($p < 0.011$). However, there were no notable differences in sex distribution, ASA classification, or BMI between the two groups. Preoperative CA 19-9 levels were comparable, averaging 237.0 ± 627.2 units/mL in the OPD group and 157.2 ± 317.7 units/mL in the MIPD group ($p = 0.111$). Regarding resectability, the OPD group was more likely to include more advanced cases, as indicated by the higher rate of BRPC ($p = 0.049$). Following propensity score matching analysis, no significant differences were observed in general characteristics, including resectability, between the two groups (Table S1).

3.2 | Perioperative Outcomes

Initially, 359 patients were included in the study (Figure 1). The disparities between the two groups aligned after PSM. The OPD group exhibited a shorter average operation time than the MIPD group (190.5 ± 257.7 min vs. 294.5 ± 222.8 min, $p = 0.002$). In the MIPD group, vascular resection and reconstruction were necessary for 23 patients (20.9%), which was comparable to the 22 patients (20.0%) in the OPD group. No significant differences were observed in the rates of intraoperative transfusion, CR-POPF, DGE, PPH, reoperation, or 30- and 90-day mortality between the groups. However, the MIPD group had a shorter hospital stay (14.8 ± 12.6 days vs. 18.9 ± 12.5 days, $p = 0.016$) (Table 2).

3.3 | Long-Term Oncologic Outcomes

Pathological characteristics and clinically significant oncological factors, such as AJCC stage, N stage, tumor size, and lymphovascular invasion (LVI), showed no differences between the two groups (Table 3). The median follow-up was 32.7 months (range 0–103) in OPD and 16.0 months (range 2–85) in the MIPD group. Throughout the follow-up period, the two groups had no significant difference in OS (OPD vs. MIPD, 38.00 ± 7.30 vs. 33.00 ± 2.00, $p = 0.670$). Similarly, disease-free survival (DFS) was comparable between the groups (OPD vs. MIPD, 15.00 ± 2.73 vs. 22.00 ± 5.25, $p = 0.179$) (Figure 2).

3.4 | General Characteristics and Perioperative Outcome in Type 0 Resection

General parameters, including sex, age, preoperative BMI, and ASA classification, showed no significant differences between the two groups (Table S2). Tumor markers and resectability were also similar between the groups. Regarding perioperative outcomes, the operation time was longer in the MIPD group than in the OPD group. However, the EBL was lower in the MIPD group, resulting in a significantly higher transfusion rate during the operation in the OPD group (9.3% vs. 2.5%) (Table S3).

3.5 | Long-Term Oncologic Outcome, Type 0 Resection

All parameters that could influence long-term oncological outcomes, such as tumor size, positive lymph nodes, AJCC 8th stage, LVI, perineural invasion, and cellular differentiation, showed no differences between the two groups (Table 4). The only exception was in the number of retrieved lymph nodes. Regarding OS, there was no statistically significant difference between the two groups (OPD vs. MIPD, 38.00 ± 5.21 vs. 34.00 ± 3.41, $p = 0.220$, Figure 3). However, there was a significant difference in DFS between the groups, with the MIPD group showing longer DFS (OPD vs. MIPD, 15.00 ± 2.36 vs. 29.00 ± 13.12, $p = 0.028$, Figure 3).

4 | Discussion

This study assessed the short- and long-term operative results of MIPD compared with those of OPD for both RPC and BRPC,

TABLE 2 | Perioperative outcome.

	Total population			Propensity-matched population		
	OPD ($N=249$)	MIPD ($N=110$)	p	OPD ($N=110$)	MIPD ($N=110$)	p
Operation time, min	190.1 ± 258.4	294.5 ± 222.8	< 0.001	230.5 ± 257.7	294.5 ± 222.8	0.002
EBL, mL	525.5 ± 818.0	341.7 ± 366.4	0.003	439.5 ± 406.7	341.7 ± 366.4	0.045
Intraoperative transfusion	29 (11.6%)	4 (3.7%)	0.019	9 (8.2%)	4 (3.7%)	0.227
Size of pancreatic duct, mm	4.3 ± 2.2	5.2 ± 2.7	0.001	4.2 ± 2.2	5.2 ± 2.7	0.002
Pancreas texture						
Soft	82 (32.9%)	36 (32.7%)	1.000	24 (28.9%)	33 (32.0%)	0.818
Hard	167 (67.1%)	74 (67.3%)		59 (71.1%)	70 (67.9%)	
Vascular resection	61 (24.5%)	24 (21.8%)	0.677	22 (20.0%)	23 (20.9%)	1.000
CR-POPF	12 (4.8%)	3 (2.7%)	0.526	7 (6.4%)	3 (2.7%)	0.332
DGE						
A	24 (9.8%)	9 (8.2%)	0.525	12 (11.1%)	9 (8.2%)	0.290
B	12 (4.9%)	2 (1.8%)		6 (5.6%)	2 (1.8%)	
C	2 (0.8%)	1 (0.9%)		0 (0.0%)	1 (0.9%)	
PPH	4 (1.6%)	1 (0.9%)	0.972	3 (2.7%)	1 (0.9%)	0.614
Reoperation	4 (1.6%)	0 (0.0%)	0.425	2 (1.8%)	0 (0.0%)	0.477
30-day mortality	1 (0.5%)	0 (0.0%)	1.000	0 (0.0%)	0 (0.0%)	1.000
90-day mortality	0 (0.0%)	0 (0.0%)	1.000	0 (0.0%)	0 (0.0%)	1.000
Hospital stays, days	17.6 ± 9.4	14.8 ± 12.6	0.039	18.9 ± 12.5	14.8 ± 12.6	0.016
Recurrence	166 (67.8%)	46 (41.8%)	< 0.001	75 (68.8%)	46 (41.8%)	< 0.001
Recurrence pattern						
Local	54 (47.4%)	6 (21.4%)	0.038	47 (46.5%)	7 (24.1%)	0.054
Distant	46 (40.4%)	18 (64.3%)		39 (38.6%)	18 (62.1%)	
Combined	13 (11.4%)	3 (10.7%)		14 (13.9%)	3 (10.3%)	
Neoadjuvant therapy	105 (42.2%)	35 (31.8%)	0.083	45 (40.9%)	35 (31.8%)	0.207
Adjuvant therapy	205 (83.0%)	90 (86.5%)	0.504	88 (80.0%)	93 (84.5%)	0.480
Period to adjuvant chemotherapy, week	7.4 ± 2.2	9.6 ± 3.8	< 0.001	7.9 ± 2.4	9.6 ± 3.8	< 0.001
R status						
R0	200 (84.7%)	91 (84.3%)	0.605	91 (86.7%)	91 (84.3%)	0.474
R1	34 (14.4%)	17 (15.7%)		13 (12.4%)	17 (15.7%)	
R2	2 (0.8%)	0 (0.0%)		1 (1.0%)	0 (0.0%)	

Abbreviations: CR-POPF, clinical relevant postoperative pancreatic fistula; DGE, delayed gastric emptying; EBL, estimated blood loss; PPH, postoperative hemorrhage.

following the mastery of the MIPD learning curve. Using PSM to analyze balanced data, the study noted that although operation times were generally longer in the MIPD group than in the OPD group, MIPD offered benefits such as quicker recovery and shorter hospitalization. Additionally, the oncological outcomes were similar to those of OPD. Specifically, in type 0 resections not involving vascular resection, although MIPD had longer operation times, it resulted in EBL and fewer intraoperative transfusions. Notably, in terms of oncological outcomes, OS was similar, but DFS was better in the MIPD group.

The findings of this study are consistent with those of previous studies in terms of short-term operative outcomes. Uijterwijk et al. conducted an individual patient data meta-analysis of four randomized trials involving 275 patients with PDAC who underwent either LPD or OPD. Analysis showed that the R0 resection

TABLE 3 | Pathologic characteristics.

	Total population			Propensity-matched population		
	OPD ($N=249$)	MIPD ($N=110$)	p	OPD ($N=110$)	MIPD ($N=110$)	p
Tumor size	2.5 ± 1.1	2.3 ± 1.0	0.109	2.4 ± 1.0	2.3 ± 1.0	0.318
Retrieved LNs	20.7 ± 10.4	17.1 ± 10.9	0.004	18.7 ± 8.7	17.1 ± 10.9	0.249
Metastatic LNs	1.9 ± 2.5	1.3 ± 2.0	0.025	1.5 ± 2.1	1.3 ± 2.0	0.417
AJCC^{8th} N stage						
N0	105 (42.2%)	55 (50.0%)	0.186	50 (45.5%)	55 (50.0%)	0.795
N1	94 (37.8%)	41 (37.3%)		45 (40.9%)	41 (37.3%)	
N2	50 (20.1%)	14 (12.7%)		15 (13.6%)	14 (12.7%)	
AJCC^{8th} stage						
IA	53 (21.3%)	25 (22.7%)	0.274	23 (20.9%)	25 (22.7%)	0.858
IB	50 (20.1%)	27 (24.5%)		26 (23.6%)	27 (24.5%)	
IIA	2 (0.8%)	3 (2.7%)		1 (0.9%)	3 (2.7%)	
IIB	94 (37.8%)	41 (37.3%)		45 (40.9%)	41 (37.3%)	
III	50 (20.1%)	14 (12.7%)		15 (13.6%)	14 (12.7%)	
LVI	106 (42.7%)	40 (36.7%)	0.341	51 (46.4%)	40 (36.7%)	0.189
PNI	188 (75.8%)	89 (81.7%)	0.279	85 (77.3%)	89 (81.7%)	0.526
Cell differentiation						
Well	36 (15.1%)	13 (11.8%)	0.294	17 (16.3%)	13 (11.8%)	0.425
Moderate	159 (66.8%)	75 (68.2%)		74 (71.2%)	75 (68.2%)	
Poor	43 (18.1%)	20 (18.2%)		13 (12.5%)	20 (18.2%)	

Abbreviations: LN, lymph node; LVI, lymphovascular invasion; PNI, perineural invasion.

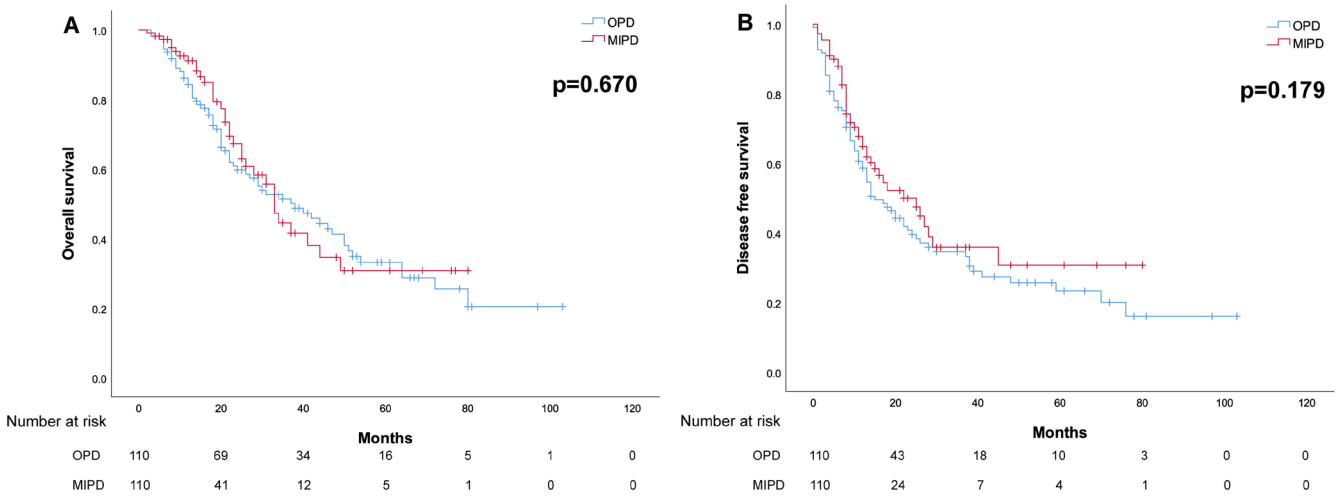

FIGURE 2 | Kaplan–Meier survival curves representing (A) overall survival and (B) disease-free survival for pancreaticoduodenectomy after propensity-score matching.

rate and lymph node yield were similar between the LPD and OPD groups. Additionally, LPD was associated with a reduced EBL and shorter hospital stay. These findings suggest that LPD is not inferior to OPD in terms of surgical radicality or short-term operative outcomes [12].

Wang et al. conducted a randomized controlled trial (RCT) comparing LPD with OPD in patients with PDAC. To address the technical complexity of LPD, only surgeons who had performed more than 104 LPDs and whose operative videos had undergone a centralized review were included in this study. Results

indicated that while laparoscopic procedures required longer operative times (330.0 [287.5–405.0] min vs. 297.0 [245.0–340.0] min; $p < 0.001$), they resulted in lower EBL compared to the OPD group (145.0 [100.0–200.0] mL vs. 200.0 [100.0–425.0] mL; $p = 0.02$). There were no significant differences in complication rates according to Clavien–Dindo grades III–IV (17 [17.0%] vs. 23 [23.0%]; $p = 0.29$) or in postoperative hospital stays (14.0 [11.0–17.0] days vs. 14.0 [12.0–18.5] days; $p = 0.37$). Although long-term oncologic outcomes were not examined in this study, the short-term operative outcomes were consistent with those reported in previous retrospective studies [5].

TABLE 4 | Pathologic characteristics in type 0 resection.

	OPD ($N = 183$)	MIPD ($N = 81$)	p
Tumor size	2.5 ± 1.1	2.2 ± 0.9	0.058
Retrieved LNs	20.6 ± 10.5	16.4 ± 11.0	0.004
Metastatic LNs	1.8 ± 2.5	1.3 ± 2.1	0.108
AJCC^{8th} N stage			
N0	82 (44.8%)	40 (49.4%)	0.316
N1	67 (36.6%)	32 (39.5%)	
N2	34 (18.6%)	9 (11.1%)	
AJCC^{8th} stage			
IA	42 (23.0%)	18 (22.2%)	0.532
IB	38 (20.8%)	20 (24.7%)	
IIA	2 (1.1%)	2 (2.5%)	
IIB	67 (36.6%)	32 (39.5%)	
III	34 (18.6%)	9 (11.1%)	
LVI	76 (41.8%)	30 (37.5%)	0.610
PNI	133 (73.1%)	67 (83.8%)	0.086
Cell differentiation			
Well	29 (16.7%)	8 (9.9%)	0.167
Moderate	113 (64.9%)	53 (65.4%)	
Poor	32 (18.4%)	18 (22.2%)	

Abbreviations: LN, lymph node; LVI, lymphovascular invasion; PNI, perineural invasion.

Jiang et al. conducted a systematic review and meta-analysis comparing LPD and OPD in the treatment of pancreatic cancer [13]. This comprehensive meta-analysis included eight studies and 15278 patients, making it the first investigation of the clinical efficacy of LPD with a focus on long-term survival outcomes. The results indicated no significant difference in 5-year OS rates (HR: 0.97, 95% CI: 0.82–1.15, $p = 0.76$). Furthermore, LPD has several advantages, such as a higher rate of complete (R0) resection, greater lymph node retrieval, shorter hospital stay, and less EBL. These findings demonstrate that LPD is comparably more effective than OPD in achieving favorable long-term oncological results.

Kwon et al. conducted a retrospective study comparing MIPD and OPD for the treatment of pancreatic cancer, involving 73 MIPD and 219 OPD patients. The findings revealed that the operative time was longer for MIPD than for OPD (392 vs. 327 min, $p < 0.001$). However, patients who underwent MIPD had shorter postoperative hospital stays than those who underwent OPD (12.4 vs. 14.2 days, $p = 0.040$). Notably, the rate of adjuvant treatment was higher in the MIPD group (80.8% vs. 59.8%, $p = 0.002$). Despite these differences, the long-term oncological outcomes did not vary significantly between the two groups [14].

All these studies explored the advantages of MIPD in terms of short-term operative outcomes compared to OPD for treating PDAC. Notably, the two groups demonstrated comparable oncological outcomes. Although the accumulation of data from expert surgeons who have overcome the learning curve solidifies these findings, the evidence remains limited to draw definitive conclusions. Nevertheless, these findings unequivocally suggest that MIPD is a viable approach to enhance the outcomes of patients with PDAC.

There is a growing need to determine which patient groups might benefit the most from MIPD as a general indication for pancreatic cancer. Beal et al.'s study, using NCDB data on 18936 patients with PDAC, suggested possible indications for MIPD, particularly noting that smaller tumors (size < 2 cm) exhibited

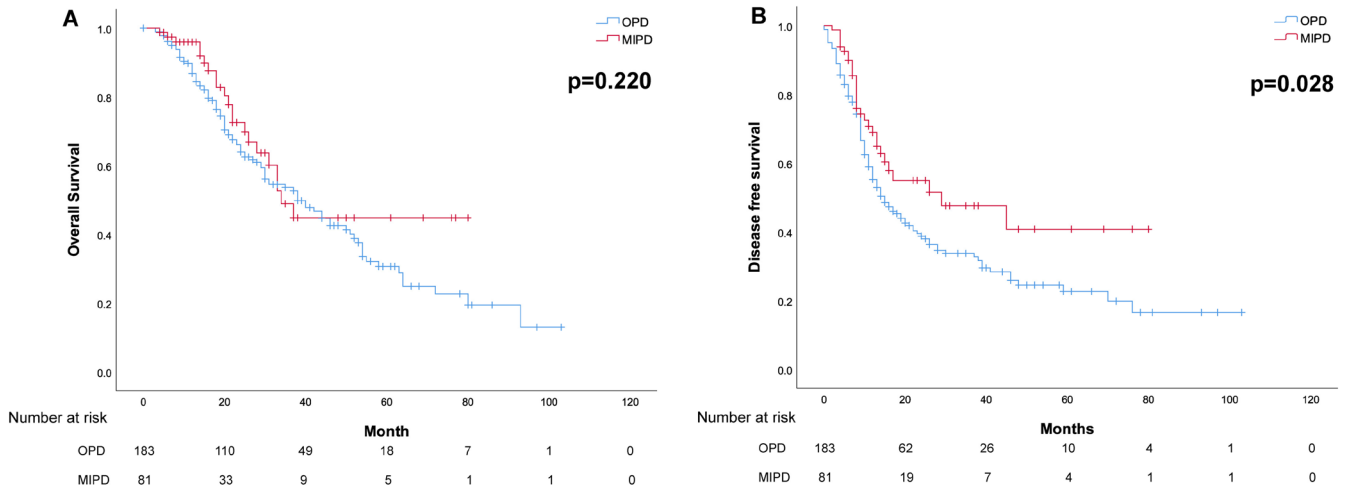

FIGURE 3 | Kaplan–Meier survival curves representing (A) overall survival and (B) disease-free survival for type 0 resection.

a higher win ratio for OS at 1.21 [15]. This aligns with the findings of this study, where type 0 MIPD, not involving vascular resection, showed better DFS. In particular, MIPD may offer the greatest benefit to patients whose tumors are confined within the pancreas with minimal desmoplastic reactions and no vascular involvement, maximizing the potential advantages of MIPD in these cases.

Previously, we proposed a model to determine when minimally invasive radical distal pancreatectomy is suitable for left-sided pancreatic cancer [16]. This model also applies to MIPD for pancreatic cancer, accounting for technical feasibility, procedural safety, and the need for margin-negative resection for optimal oncological outcomes [17]. The surgeon's technical abilities should be adequate to achieve the surgical range necessary for curative intent. Our study highlights that the group that underwent type 0 resection (including standard lymphadenectomy without vascular resection) experienced better short-term operative outcomes and improved DFS.

The justification for standard lymphadenectomy being sufficient in pancreatic cancer stems from its role as a critical prognostic factor; over half of resected pancreatic cancers exhibit lymph node metastasis, correlating with poorer survival rates. Whether extended lymphadenectomy should be performed alongside resection for pancreatic cancer remains unclear. Many retrospective and observational studies have suggested that extended dissections that include the superior mesenteric artery, celiac trunk, and para-aortic lymph nodes should be performed [18, 19]. However, the potential for selection bias in these studies warrants cautious interpretation of their findings. Several prospective RCTs have been conducted to determine the optimal scope of surgical resection. A meta-analysis reviewing oncological outcomes from five RCTs that compared extended and standard lymphadenectomies in patients undergoing PD showed that PD with standard lymphadenectomy was safer, as evidenced by shorter operation times, fewer transfusions, fewer overall postoperative complications, and similar rates of complete tumor removal (R0). Additionally, the long-term survival outcomes were comparable to those of extended lymphadenectomy [Hazard ratio: 1.01, 95% CI: 0.77–1.34, $p = 0.923$] [20].

Type 0 resection is considered an optimal indication for MIPD because it generally results in a lower EBL and fewer intraoperative transfusions than OPD. Previous studies suggest that fewer transfusions may influence postoperative complications and long-term oncologic outcomes, potentially impacting both short- and long-term surgical results [21]. Furthermore, our research showed that although the MIPD group required a longer time to commence adjuvant chemotherapy than the OPD group, they still demonstrated favorable outcomes. Recently, high-volume centers have performed MIPD using portovenous resection. However, the applicability of these results to broader patient populations has not been demonstrated [22, 23]. Therefore, for patients diagnosed with RPC or BRPC, considering MIPD over OPD may be a viable option when type 0 resection is feasible.

In our cohort, MIPD was associated with improved DFS while OS remained comparable to OPD. Interestingly, a similar trend of prolonged DFS without OS benefit had also been observed in our previous study [17]. At that time, we attributed the finding to the relatively short follow-up duration. However, given that this pattern continues to be observed with longer follow-up, it may indicate a potential oncologic relevance of type 0 resection in the MIPD setting. Although recurrence has traditionally been regarded as a surrogate marker for OS, recent advances may have attenuated this relationship in pancreatic cancer. The development of effective second-line agents, improvements in patients' general condition, and the widespread implementation of best supportive and palliative care likely contribute to the lack of OS difference despite better DFS in the MIPD group. Moreover, minimally invasive approaches have been linked to attenuated postoperative systemic inflammation and better immune preservation (lower IL-6/CRP), which could plausibly delay micrometastatic progression and prolong DFS without necessarily extending OS once salvage treatments are administered.

Although adjuvant therapy began later in the MIPD group, prior studies suggest that moderate delays within typical postoperative windows do not consistently compromise OS, whereas the adequacy of systemic therapy may be more prognostic [24, 25]. In addition, we evaluated the completion of adjuvant chemotherapy according to standard definitions (gemcitabine ≥ 6 cycles, modified FOLFIRINOX ≥ 12 cycles). Completion rates of adjuvant chemotherapy were comparable between OPD and MIPD in both the total population (Gemcitabine 61.1% vs. 67.4%, FOLFIRINOX 27.3% vs. 37.5%) and the PSM population (59.6% vs. 67.4%, 20.7% vs. 37.5%), with no significant differences observed (Table S5). These results indicate that MIPD did not compromise the delivery of systemic therapy compared with OPD.

This study had several limitations. As a single-center retrospective study with a small sample size, there is a risk of undetected selection bias. Additionally, variations in the modalities of preoperative and postoperative chemotherapy, influenced by the patient's condition and physician's judgment, could limit the study's findings. Another limitation of our study is the lack of objective data on periarterial divestment. Although standard dissection is routinely performed in our center, periarterial tissue stripping was occasionally required in BRPC cases that underwent type 0 resection after neoadjuvant therapy. The fact that most BRPC patients proceeded to surgery only after regression following systemic therapy may have introduced a degree of selection bias. Future prospective data collection will be necessary to clarify the oncological relevance of periarterial divestment and the potential impact of selection bias in this setting. Therefore, RCTs are necessary to clarify the oncological outcomes and survival rates associated with MIPD in the treatment of PDAC.

In conclusion, MIPD for RPC and BRPC showed comparable short-term operative and long-term oncological outcomes in well-selected patient groups, indicating that MIPD is not inferior to OPD. Specifically, the type 0 resection group demonstrated superior short- and long-term oncological outcomes, suggesting that type 0 resection should be considered the optimal indication for MIPD when feasible.

Author Contributions

Conception and design: Munseok Choi and Chang Moo Kang; administrative support: Ho Kyoung Hwang; collection and assembly of data:

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Research data are not shared.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Patient characteristics. **Table S2:** Patient

characteristics in type 0 resection. **Table S3:** Perioperative outcome in type 0 resection. **Table S4:** Combined organ resections in OPD and MIPD groups (total vs. PSM populations). **Table S5:** Completion of adjuvant chemotherapy (Gemcitabine ≥ 6 cycles, FOLFIRINOX ≥ 12 cycles). **Figure S1:** Annual case distribution of open (OPD), laparoscopic (LPD), and robot-assisted laparoscopic pancreatoduodenectomy (RALPD) between 2014 and 2022. **Figure S2:** Annual case distribution of open pancreatoduodenectomy (OPD), laparoscopic pancreatoduodenectomy (LPD), and robot-assisted laparoscopic pancreatoduodenectomy (RALPD) performed at Severance Hospital between 2014 and 2024.