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Effects of Minimally Invasive Versus Open Pancreatoduodenectomy on Short-Term Surgical Outcomes and Postoperative Nutritional and Immunological Statuses

A Single-Institution Propensity Score-Matched Study

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Objective: To evaluate the feasibility and clinical impact of minimally invasive pancreatoduodenectomy (MIPD) versus open pancreatoduodenectomy (OPD) on postoperative nutritional and immunological indices.

Background: The surgical advantages of MIPD over OPD are controversial, and the postoperative nutritional and immunological statuses are unknown.

Methods: In total, 306 patients who underwent MIPD (n = 120) or OPD (n = 186) for periampullary tumors from April 2016 to February 2024 were analyzed. Surgical outcomes and postoperative nutritional and immunological indices (albumin, prognostic nutritional index [PNI], neutrophil-to-lymphocyte ratio [NLR], and platelet-to-lymphocyte ratio [PLR]) were examined by 1:1 propensity score matching (PSM) with well-matched background characteristics.

Results: PSM resulted in 2 balanced groups of 99 patients each. Compared with OPD, MIPD was significantly associated with less estimated blood loss ($P < 0.0001$), fewer intraoperative blood transfusions ($P = 0.001$), longer operative time, shorter postoperative hospital stay ($P < 0.0001$), fewer postoperative complications ($P = 0.001$) (especially clinically relevant postoperative pancreatic fistula [$P = 0.018$]), and a higher rate of textbook outcome achievement (70.7% vs 48.5%, $P = 0.001$). The number of dissected lymph nodes and the R0 resection rate did not differ between the 2 groups. In elective cases with textbook outcome achievement, the change rates of albumin, PNI, NLR, and PLR from before to after surgery were equivalent in both groups.

Conclusions: MIPD has several surgical advantages (excluding a prolonged operative time), and it enhances the achievement of textbook outcomes over OPD. However, the postoperative nutritional and immunological statuses are equivalent for both procedures.

Keywords: minimally invasive pancreatoduodenectomy, nutritional and immunological status, open pancreatoduodenectomy, pancreatic fistula, postoperative complications, textbook outcome

INTRODUCTION

Pancreatoduodenectomy (PD) is the classic curative surgery for resectable periampullary tumors. Despite the recent development of surgical instruments and improvement of surgical techniques for pancreatic surgery, PD is still associated with a high risk of postoperative complications such as pancreatic fistula or bleeding, with incidence rates reaching 50%.[1,2]

Minimally invasive PD (MIPD), including laparoscopic, robot-assisted, and hybrid techniques, has been widely implemented during the past decade. Several studies, including 4 randomized clinical trials (RCTs), have been performed in an attempt to elucidate the clinical benefits of MIPD. In systematic reviews and meta-analyses of nonrandomized retrospective studies or nationwide studies between MIPD and open PD (OPD), MIPD showed better short-term nononcologic

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The datasets generated during and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

The protocol for this retrospective research has been approved by a suitably constituted Ethics Committee of the institution, and it conforms to the provisions of the Declaration of Helsinki. The Ethics Committee of the Graduate School of Medicine, Kumamoto University (Kumamoto, Japan).

Informed consent was obtained from all human subjects according to institutional guidelines.

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outcomes (such as lower blood loss and shorter hospital stay) as well as oncological noninferiority compared with OPD.[3–11] Additionally, 2 single-center and 1 multicenter RCT comparing laparoscopic PD (LPD) versus OPD for periampullary tumors revealed a shorter length of hospital stay (LOS) in the laparoscopic approach and equivalent pancreas-specific morbidity between the 2 approaches.[12–14] However, the LEOPARD-2 trial was prematurely ended because of the higher 90-day complication-related mortality rate with LPD than with OPD.[15] Thus, the true impact of MIPD on surgical outcomes remains unclear. OPD is still one of the most invasive gastrointestinal surgeries. If MIPD provides benefits of decreased pain, shorter hospitalization, reduced postoperative complications, and enhanced recovery after surgery, the postoperative nutritional and immunological statuses also may be enhanced. Unfortunately, studies focusing on postoperative nutritional and immunological statuses are lacking.

In the present study, we compared MIPD and OPD for periampullary tumors with respect to the short-term surgical outcomes and clinical impact on the postoperative nutritional and immunological statuses using a propensity score-matching (PSM) analysis.

METHODS

Study Design

We conducted a single-center retrospective study comparing MIPD and OPD in a PSM cohort. All patients provided written informed consent, and the Ethics Committee of Kumamoto University approved the study protocol. The institutional ethical review board approved this study (IRB no. 1800), and all procedures were performed in accordance with the guidelines of the Declaration of Helsinki.

Eligibility and Data Collection

This study involved 334 consecutive patients with periampullary tumors who underwent MIPD or OPD at Kumamoto University Hospital from April 2016 to February 2024. The indications for MIPD in our institution were as follows: body mass index (BMI) of <30 kg/m^2, no severe organ disorders (eg, cardiopulmonary dysfunction, blood disorders, dialysis), no history of upper mesocolic abdominal surgeries, no evidence of major vascular involvement on preoperative imaging, and no need for combined resection of other organs. OPD did not have such a limited operative indication. Patients who underwent conversion from MIPD to OPD were included in the OPD group. The exclusion criteria were combined resection for lesions in other organs, combined artery resection with revascularization, emergency PD, a history of pancreatectomy, insufficient baseline data, or missing primary outcome data.

Variables and Definitions

The patients' baseline characteristics, operation-related parameters, short-term surgical outcomes, and nutritional and immunological status indices were collected from the medical records.

The resection margins were defined by the pathologists in our institution. The margin status was considered R1 when the distance between the tumor and any resection margins was ≤1 mm and R2 when macroscopic tumor tissue remained. Pathological TNM and stage were classified according to the 8th edition of the Union for International Cancer Control staging system. Resectability (resectable, borderline resectable, or unresectable) of pancreatic ductal adenocarcinoma (PDAC) was assessed according to the National Comprehensive Cancer Network guidelines (version 2.2021). Postoperative complications were defined as Clavien–Dindo classification (CD-c) grade ≥IIIa complications occurring within 90 days after surgery.[16] Pancreas-specific complications, including postoperative pancreatic fistula (POPF), postpancreatectomy hemorrhage (PPH), and delayed gastric emptying (DGE), were defined in accordance with the International Study Group of Pancreatic Surgery,[17–19] which defines clinically relevant POPF (CR-POPF) as grade B or C.[17] Bile leakage was defined according to the International Study Group of Liver Surgery.[20] Postoperative mortality was defined as the number of deaths occurring within 30 days after surgery.

Indices of the nutritional and immunological statuses were defined as the albumin concentration, postoperative prognostic nutritional index (PNI),[21] neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). Postoperative albumin, PNI, NLR, and PLR were calculated from the blood tests that were performed when the patients visited our hospital for the first routine follow-up after surgery (approximately 30–60 days postoperatively). To assess changes in the nutritional and immunological statuses from before to after surgery, the percent change in the preoperative and postoperative nutrition scores was calculated as follows: percent change (%) = (postoperative score – preoperative score)/preoperative score. Albumin, PNI, NLR, and PLR index were defined as the percent change in each. Textbook outcomes were defined according to a previous report.[22]

Statistical Analysis

Continuous variables are expressed as mean ± SD or median with interquartile range according to the data type (parametric or nonparametric, respectively) and analyzed using the Wilcoxon signed-rank test or Mann–Whitney test. Categorical variables were evaluated using the chi-square test or Fisher exact test as appropriate. To reduce the bias arising from patient selection and lack of randomization, PSM was performed with 1:1 nearest-neighbor matching[23] using a caliper width of 0.2. A logistic regression model with well-known variables potentially affecting the outcomes was used to estimate the propensity score. The outcomes were then compared between the OPD and MIPD groups in the matched cohort.

We calculated the 95% confidence intervals, and $P < 0.05$ was considered statistically significant. All statistical analyses were performed using JMP Pro software version 16.0.0 (SAS Institute, Cary, NC).

RESULTS

Clinicopathological Characteristics and Perioperative Outcomes Before PSM

A total of 306 patients met the inclusion criteria and were analyzed (Fig. 1). Among these patients, MIPD was planned for 128, but 8 (6.3%) required conversion to OPD. Therefore, we analyzed 186 (60.8%) patients who underwent OPD and 120 (39.2%) who underwent MIPD. The reasons for conversion were the need for vascular resection (n = 5, 62.5%), treatment of inflammation-induced peripancreatic adhesions (n = 2, 25.0%), and management of intraoperative bleeding (n = 1, 12.5%). In the MIPD group, LPD and robot-assisted PD (RPD) were performed in 81 (67.5%) and 39 (32.5%) patients, respectively.

The demographics, clinicopathological characteristics, and perioperative outcomes in the unmatched cohort are summarized in Table 1. There were no differences in sex, age, BMI, Eastern Cooperative Oncology Group performance status (ECOG PS), American Society of Anesthesiologists (ASA) score, history of diabetes, cholangitis, pancreatitis, preoperative biliary drainage, or preoperative chemotherapy between the 2 groups. Compared with the OPD group, the MIPD group had a higher incidence of soft pancreas (75.8% vs 47.3%, $P < 0.0001$) and

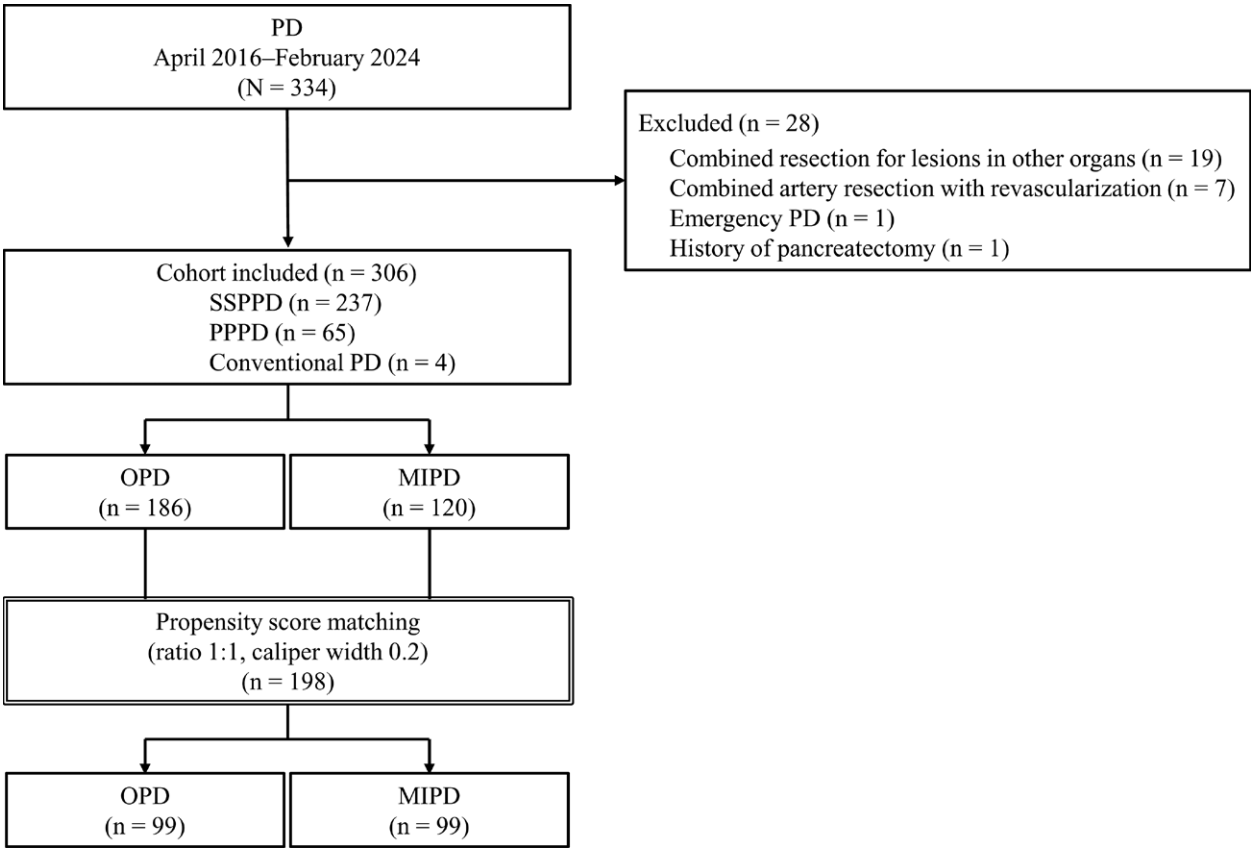

FIGURE 1. Flowchart of surgical outcomes analysis. PPPD indicates pylorus-preserving pancreatoduodenectomy; SSPPD, subtotal stomach-preserving pancreatoduodenectomy.

a lower incidence of concomitant vascular resection (7.5% vs 23.1%, $P < 0.0001$). The details of vascular resection were as follows: segmental resection with end-to-end anastomosis (n = 43), wedge resection with primary closure (n = 5), reconstruction using venous interposition allograft (n = 2), and other procedures (n = 2) in our cohort. Regarding postoperative outcomes, the MIPD group had a significantly longer median operative time (524 [476–591] vs 473 [411–554] min, $P < 0.0001$) and significantly lower median estimated blood loss (EBL) (303 [150–543] vs 612 [356–1057] g, $P < 0.0001$) than the OPD group. Moreover, a shorter LOS was seen in the MIPD group (15.0 [11.0–23.0] vs 25.0 [17.0–38.3] days, $P < 0.0001$). The total postoperative complication rate (CD-c grade ≥IIIa) was lower in the MIPD group (29.2% vs 41.4%, $P = 0.030$); however, pancreas-specific complications were comparable between the 2 groups, including the rates of CR-POPF (28.3% vs 36.0%, $P = 0.163$), PPH (6.7% vs 5.9%, $P = 0.790$), and DGE (1.7% vs 4.3%, $P = 0.206$). Postoperative pathologic examination revealed lower rates of malignancies (74.2% vs 88.7%, $P = 0.001$) and PDAC (23.3% vs 39.3%, $P = 0.004$) as well as smaller tumors in the MIPD than OPD group. No mortality occurred within 30 days postoperatively in either group.

Clinicopathological Characteristics and Perioperative Outcomes After PSM

The following variables, well known to affect outcomes, were used for PSM: sex, age, BMI, ECOG PS, ASA score, preoperative chemotherapy, pathological malignancy, pathological PDAC, tumor diameter, soft pancreas, and concomitant vascular resection. After PSM, 198 patients were correctly matched (99 patients in each group) (Fig. 1). The clinicopathological characteristics and perioperative outcomes in the matched cohort are shown in Table 2. No significant differences were evident between the 2 groups in the matched cohort in terms of baseline characteristics, postoperative pathological diagnosis, concomitant vascular resection, and pancreatic texture. All vascular resections were segmental resections of portal vein/superior mesenteric vein (9 cases in MIPD and 8 cases in OPD). In the PDAC patients, stage classifications and resectability (resectable/borderline resectable/unresectable) are also not significantly different in both groups after PSM (Supplemental Table 1, see http://links.lww.com/AOSO/A399). In the MIPD group, LPD and RPD were performed in 70 (70.7%) and 29 (29.3%) patients, respectively. Regarding postoperative outcomes, the median operative time was significantly longer (523 [476–594] vs 458 [342–549] min, $P = 0.001$) and the median EBL was significantly lower (330 [175–550] vs 611 [350–1060] g, $P < 0.001$) in the MIPD than OPD group. Additionally, the MIPD group was less likely to require intraoperative blood transfusion (6.1% vs 23.2%, $P = 0.001$). Moreover, the MIPD group had a shorter LOS (15.0 [11.0–23.0] vs 27.0 [17.0–41.0] days, $P < 0.0001$) and lower total postoperative complication rate (CD-c grade ≥IIIa) (29.3% vs 51.5%, $P = 0.001$). In particular, the CR-POPF rate was significantly lower in the MIPD group (28.3% vs 44.4%, $P = 0.018$). The incidence of PPH (8.1% vs 10.1%, $P = 0.621$), DGE (2.0% vs 3.0%, $P = 0.312$), and bile leakage (0.0% vs 1.0%, $P = 0.316$) were comparable between the 2 groups. The number of dissected lymph nodes (18.0 [10.5–27.5] vs 19.0 [9.0–27.0], $P = 0.834$) and the rate of R0 resection (91.9% vs 85.9%, $P = 0.175$) were also comparable, suggesting that the oncological outcomes of MIPD are comparable to those of OPD. No 30-day mortality was seen in either group. Additionally, higher rates of achieving textbook outcomes were observed in the MIPD group (70.7% vs 48.5%, $P = 0.018$).

TABLE 1.

Clinicopathological Characteristics and Perioperative Outcomes Before PSM

Characteristic	OPD n = 186	MIPD n = 120	*P*
Male (%)	115 (61.8%)	69 (57.5%)	0.450
Age (yr), mean ± SD	68.9 ± 9.5	67.9 ± 12.3	0.831
BMI, mean ± SD	22.5 ± 3.4	23.0 ± 3.4	0.106
ECOG PS ≤1 (%)	179 (96.2%)	116 (96.7%)	0.844
ASA score ≤2 (%)	154 (82.8%)	106 (88.3%)	0.188
Surgical approach			—
Laparoscopic (%)	—	81 (67.5%)	
Robotic (%)	—	39 (32.5%)	
History of diabetes (%)	69 (37.1%)	46 (38.3%)	0.827
History of cholangitis (%)	31 (16.7%)	22 (18.3%)	0.707
History of pancreatitis (%)	8 (4.3%)	7 (5.8%)	0.544
Preoperative biliary drainage (%)	75 (40.3%)	39 (32.5%)	0.167
Preoperative chemotherapy (%)	32 (17.2%)	23 (19.2%)	0.663
Malignancy (%)	165 (88.7%)	89 (74.2%)	0.001
PDAC (%)	73 (39.3%)	28 (23.3%)	0.004
Other malignancy			0.479
Pancreatic cancer (excluding PDAC) (%)	30 (16.1%)	13 (10.3%)	
Biliary tract cancer (%)	53 (28.5%)	42 (35.0%)	
Duodenal cancer (%)	9 (4.8%)	6 (5.0%)	
Tumor diameter (mm), median (IQR)	30.0 (19.0–40.0)	24.0 (13.0–33.0)	0.002
Soft pancreas (%)	88 (47.3%)	91 (75.8%)	<0.0001
Vascular resection (%)	43 (23.1%)	9 (7.5%)	<0.0001
Operative time (min), median (IQR)	473 (411–554)	524 (476–591)	<0.0001
Estimated blood loss (g), median (IQR)	612 (356–1057)	303 (150–543)	<0.0001
Intraoperative blood transfusion (%)	44 (23.7%)	6 (5.0%)	<0.0001
Number of dissected lymph nodes, median (IQR)	20 (10–27)	17 (9–27)	0.335
R0 resection (%)	154 (82.8%)	110 (91.7%)	0.028
Length of hospital stay (d), median (IQR)	25.0 (17.0–38.3)	15.0 (11.0–23.0)	<0.0001
Postoperative complications (CD-c ≥IIIa) (%)	77 (41.4%)	35 (29.2%)	0.030
CR-POPF (%)	67 (36.0%)	34 (28.3%)	0.163
PPH (%)	11 (5.9%)	8 (6.7%)	0.790
DGE (%)	8 (4.3%)	2 (1.7%)	0.206
Bile leakage (%)	1 (0.5%)	0 (0.0%)	0.421
30-d mortality (%)	0 (0.0%)	0 (0.0%)	1.0
Textbook outcomes achieved (%)	109 (58.6%)	85 (70.8%)	0.030

IQR indicates interquartile range; PPH, postpancreatectomy hemorrhage.

Comparison of Postoperative Nutritional and Immunological Statuses Between MIPD and OPD

We assessed the postoperative nutritional and immunological statuses in patients who achieved textbook outcomes to exclude the effect of postoperative complications (Fig. 2).[22] For this purpose, we focused on the percent change of well-known nutritional indices (albumin, PNI, NLR, and PLR) before and after surgery. The following variables, well known to affect outcomes, were used for PSM: sex, age, BMI, ECOG PS, ASA score, preoperative chemotherapy, pathological malignancy, pathological PDAC, and concomitant vascular resection.

The clinical characteristics and perioperative outcomes before and after PSM are summarized in Supplemental Table 2, see http://links.lww.com/AOSO/A399 and Table 3, respectively. The baseline characteristics were not different between the 2 groups in the matched cohort. Interestingly, the data regarding the achievement of textbook outcomes also demonstrated the superiority of MIPD over OPD in terms of EBL and LOS, suggesting that these advantages of MIPD do not depend on the rate of postoperative complications. However, despite the advantages of MIPD, no significant difference in any nutritional score was found between the 2 groups (albumin index: $P = 0.911$, PNI: $P = 0.895$, NLR index: $P = 0.935$, PLR index: $P = 0.626$) (Fig. 3). Additionally, in the PSM analysis of the total cohort, the postoperative nutritional and immunological status indices were also comparable between the 2 groups (data not shown).

DISCUSSION

This single-center PSM study revealed that MIPD had better short-term surgical outcomes than OPD in terms of EBL, intraoperative blood transfusion, LOS, postoperative complications (especially CR-POPF), and achievement of textbook outcomes. Moreover, MIPD was equivalent to OPD in oncologic outcomes such as the number of dissected lymph nodes and the rate of R0 resection. Unexpectedly, despite these advantages of MIPD, no advantages were found in terms of the postoperative nutritional and immunological statuses, even in the cohort that achieved textbook outcomes. These results suggest the importance of not only the surgical approach but also the use of alternative therapeutic strategies to achieve enhanced postoperative nutritional and immunological statuses after PD.

Many recent studies have compared the surgical outcomes between MIPD and OPD. However, the advantages of MIPD in terms of postoperative surgical outcomes remain controversial. Previous studies, including single-institution reports, systematic reviews, and meta-analyses, have produced varying results. Some have shown that MIPD has advantages in terms of LOS, EBL, and postoperative complications,[4,10,11] whereas others did not show all of these advantages.[5–8,24–30] Notably, 3 RCTs revealed advantages of MIPD in terms of LOS and EBL,[12–14] whereas only one study showed an advantage of MIPD in terms of postoperative complications.[13] The abovementioned RCTs and the present PSM analysis suggest that MIPD facilitates shorter LOS and less EBL. Additionally, the present study suggests that postoperative complications, including POPF, are less likely to

TABLE 2.

Clinicopathological Characteristics and Perioperative Outcomes After PSM

Characteristic	OPD n = 99	MIPD n = 99	*P*
Male (%)	55 (55.6%)	61 (61.6%)	0.387
Age (yr), mean ± SD	69.5 ± 9.3	68.4 ± 11.6	0.566
BMI, mean ± SD	23.1 ± 3.6	23.0 ± 3.1	0.934
ECOG PS ≤1 (%)	96 (97.0%)	95 (96.0%)	0.700
ASA score ≤2 (%)	84 (84.9%)	86 (86.9%)	0.683
Surgical approach			—
Laparoscopic (%)	—	70 (70.7%)	
Robotic (%)	—	29 (29.3%)	
History of diabetes (%)	30 (30.3%)	37 (37.4%)	0.293
History of cholangitis (%)	17 (17.2%)	21 (21.2%)	0.470
History of pancreatitis (%)	5 (5.1%)	5 (5.1%)	1.0
Preoperative biliary drainage (%)	37 (37.4%)	37 (37.4%)	1.0
Preoperative chemotherapy (%)	19 (19.2%)	21 (21.2%)	0.723
Malignancy (%)	83 (83.8%)	84 (84.9%)	0.845
PDAC (%)	24 (24.2%)	27 (27.3%)	0.626
Other malignancy			0.684
Pancreatic cancer (excluding PDAC) (%)	18 (18.2%)	13 (13.1%)	
Biliary tract cancer (%)	33 (33.3%)	38 (38.4%)	
Duodenal cancer (%)	8 (8.1%)	6 (6.1%)	
Tumor diameter (mm), median (IQR)	28.0 (17.0–40.0)	25.0 (14.0–35.0)	0.400
Soft pancreas (%)	69 (69.7%)	70 (70.7%)	0.877
Vascular resection (%)	8 (8.1%)	9 (9.1%)	0.800
Operative time (min), median (IQR)	458 (342–549)	523 (476–594)	0.001
Estimated blood loss (g), median (IQR)	611 (350–1060)	330 (175–550)	<0.0001
Intraoperative blood transfusion (%)	23 (23.2%)	6 (6.1%)	0.001
Number of dissected lymph nodes, median (IQR)	19.0 (9.0–27.0)	18.0 (10.5–27.5)	0.834
R0 resection (%)	85 (85.9%)	91 (91.9%)	0.175
Length of hospital stay (d), median (IQR)	27.0 (17.0–41.0)	15.0 (11.0–23.0)	<0.0001
Postoperative complications (CD-c ≥IIIa) (%)	51 (51.5%)	29 (29.3%)	0.001
CR-POPF (%)	44 (44.4%)	28 (28.3%)	0.018
PPH (%)	10 (10.1%)	8 (8.1%)	0.621
DGE (%)	3 (3.0%)	2 (2.0%)	0.312
Bile leakage (%)	1 (1.0%)	0 (0.0%)	0.316
30-d mortality (%)	0 (0.0%)	0 (0.0%)	1.0
Textbook outcomes achieved (%)	48 (48.5%)	70 (70.7%)	0.001

IQR indicates interquartile range; PPH, postpancreatectomy hemorrhage.

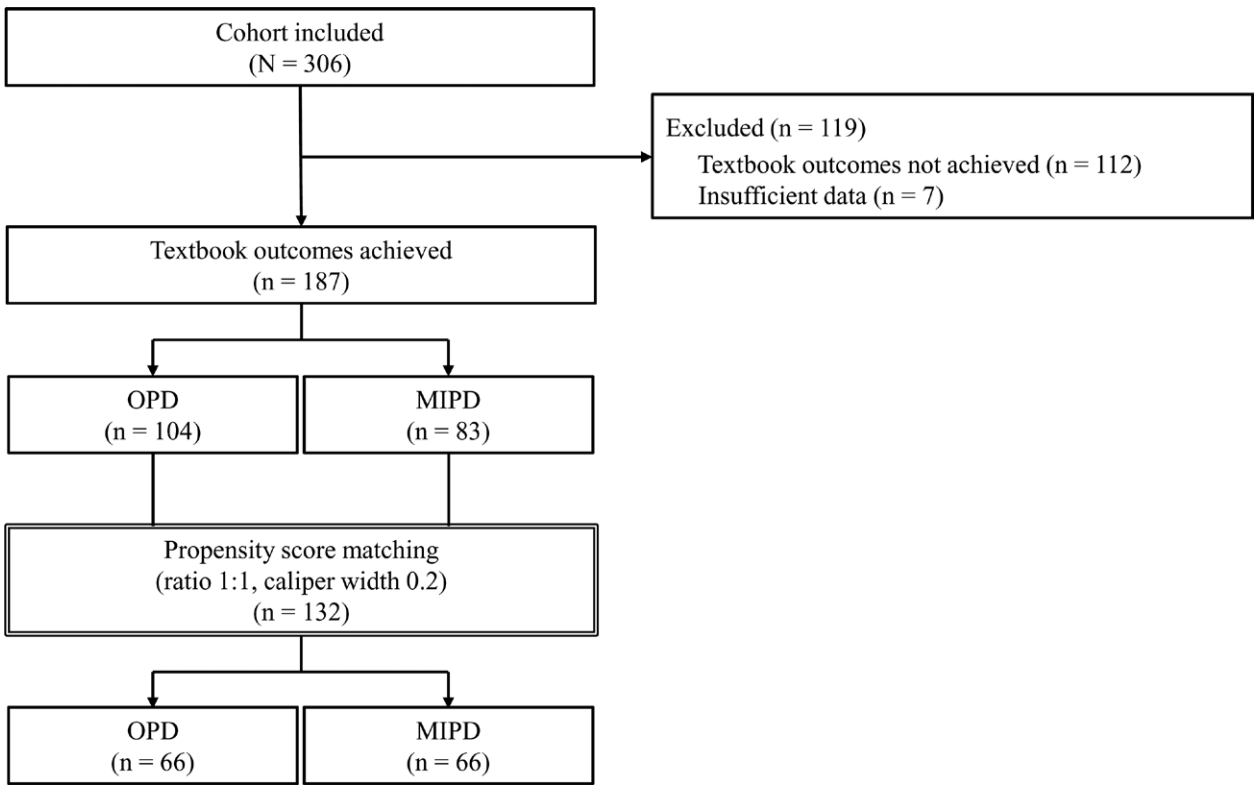

FIGURE 2. Flowchart of textbook outcome analysis.

TABLE 3.

Post-PSM Clinicopathological Characteristics and Perioperative Outcomes in Patients Who Achieved Textbook Outcomes

Characteristic	OPD n = 66	MIPD n = 66	*P*
Male (%)	37 (56.1%)	37 (56.1%)	1.0
Age (year), mean ±SD	69.4 ± 9.2	70.1 ± 8.7	0.911
BMI, mean ± SD	22.4 ± 3.2	22.5 ± 3.3	0.875
ECOG PS ≤1 (%)	63 (95.5%)	64 (97.0%)	0.648
ASA score ≤2 (%)	61 (92.4%)	61 (92.4%)	1.0
Surgical approach			—
Laparoscopic (%)	—	40 (60.6%)	
Robotic (%)	—	26 (39.3%)	
Preoperative diabetes (%)	42 (63.6%)	36 (54.6%)	0.288
Preoperative chemotherapy (%)	16 (24.2%)	15 (22.7%)	0.837
Malignancy (%)	59 (89.4%)	57 (86.4%)	0.594
PDAC (%)	20 (30.3%)	21 (31.8%)	0.851
Other malignancy			0.215
Pancreatic cancer (excluding PDAC) (%)	19 (28.8%)	10 (15.2%)	
Biliary tract cancer (%)	18 (27.3%)	21 (31.8%)	
Duodenal cancer (%)	2 (3.0%)	5 (7.6%)	
Vascular resection (%)	11 (16.7%)	9 (13.6%)	0.627
Operative time (min), median (IQR)	456 (406 to 539)	522 (476 to 569)	0.002
Estimated blood loss (g), median (IQR)	556 (317 to 934)	301 (122 to 550)	<0.0001
Intraoperative blood transfusion (%)	14 (21.2%)	3 (4.6%)	0.004
Length of hospital stay (d), median (IQR)	18.0 (14.0 to 23.3)	14.0 (11.0 to 17.3)	<0.0001
Albumin index (%), median (IQR)	–6.4 (–16.7 to 3.3)	–6.5 (–16.3 to 3.3)	0.911
PNI index (%), median (IQR)	–4.0 (–13.8 to 3.5)	–3.2 (–15.3 to 4.2)	0.895
NLR index (%), median (IQR)	–4.7 (–30.4 to 56.6)	0.2 (–37.2 to 50.4)	0.935
PLR index (%), median (IQR)	13.2 (–17.8 to 57.3)	12.9 (–17.6 to 49.1)	0.626

IQR indicates interquartile range.

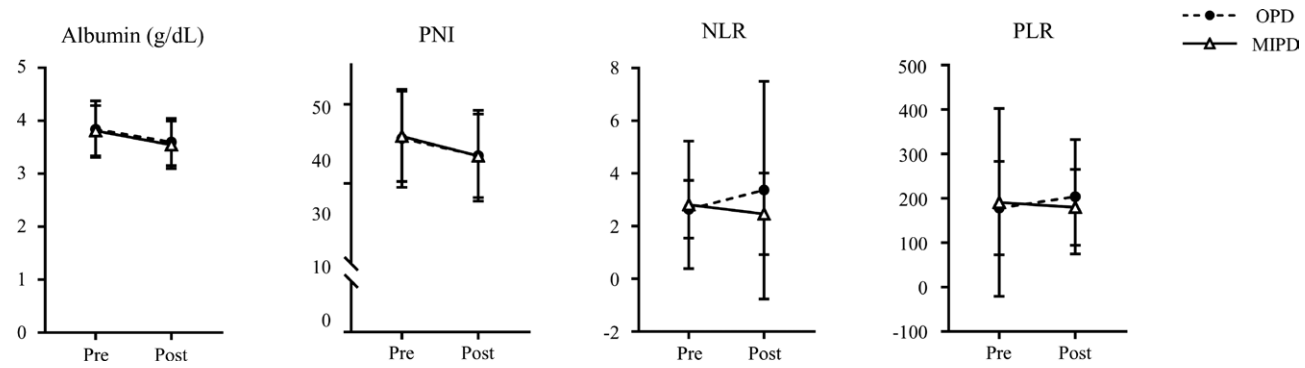

FIGURE 3. Preoperative and postoperative changes in nutritional and immunological statuses.

occur with MIPD. We consider there are 3 reasons why MIPD has better short-term surgical outcomes than OPD. First, MIPD provides a magnified view and enables precise tissue manipulation in anastomosis. Second, MIPD can reduce the development of bowel wall edema after laparoscopy compared to OPD,[31] resulting in better anastomotic healing. Moreover, a reduction in the development of bowel wall edema can lead to enhanced gastrointestinal peristalsis and oral intake early after surgery. Third, a smaller skin incision in MIPD can reduce postoperative pain and promote early postoperative rehabilitation, which also contributes to preventing POPF formation. Interestingly, MIPD was associated with a higher rate of achieving textbook outcomes than was OPD in the present study, suggesting that MIPD enhances social reintegration. The MIPD procedures in the present study included both LPD and RPD, whereas the abovementioned RCTs only included LPD. This difference may have contributed to the minor discrepancy in surgical outcomes between the present study and the above RCTs. Unfortunately, the LEOPARD-2 trial,[15] a multicenter RCT, was prematurely terminated because of the higher 90-day complication-related mortality rate among the patients undergoing LPD than OPD. Given this outcome, the role of MIPD remains a subject of debate. Although no RCTs to date have focused on RPD, a recent systematic review and meta-analysis showed no difference in surgical outcomes between RPD and LPD.[32–34] Further multicenter RCTs that include RPD may be required to elucidate the true superiority of MIPD over OPD. In our series, the conversion rate was 6.8%, which was much lower than that of many other series (3.8%–26.0%).[13,15,26,32,35–38] Moreover, the reasons for conversion to OPD in the present study were mainly adhesion and tumor-related factors such as vascular invasion. Only one (0.78%) patient required conversion because of intraoperative bleeding. These results indicate that MIPD is feasible. However, it is still difficult to discern the necessity of vascular resection on preoperative images, especially in cases of PDAC with preoperative chemotherapy. RPD with vascular resection and reconstruction may be the next step to decrease the need for conversion to OPD in the near future.

With respect to oncological outcomes, the number of dissected lymph nodes and the rate of R0 resection were comparable between the 2 groups in the matched cohort. However, no strong conclusions regarding oncologic outcomes can be drawn

from this study because of its limited power and the heterogeneity of the patients' diseases, including benign tumors and malignancies.

Achievement of textbook outcomes as a novel quality measure in pancreatic surgery has recently become a research hotspot.[22] In previous studies, textbook outcomes were achieved in 58.3% to 59.0% of patients with every PD approach, 55.0% with OPD, and 46.4% to 85.0% with MIPD.[22,39–41] In our unmatched cohort, 60.7% of patients who underwent all PD approaches, 55.7% of those who underwent OPD, and 69.2% of those who underwent MIPD achieved textbook outcomes. In our matched cohort, the rate of textbook outcome achievement was 47.4% in OPD and 71.1% in MIPD. The rate of textbook outcome achievement with OPD in the matched cohort was inferior to that in the unmatched cohort. This may have occurred because the OPD group in the matched cohort included more patients with benign tumors than did OPD groups in previous reports. Indeed, PDAC was associated with a higher rate of achieving textbook outcomes.[22] Collectively, our results revealed a significantly higher rate of textbook outcome achievement with MIPD than with OPD, which might enhance social reintegration after surgery.

Such enhanced recovery with MIPD over OPD led us to hypothesize that MIPD improves postoperative nutritional and immunological statuses. Few studies have investigated the advantages of MIPD in terms of the postoperative nutritional status. Chen et al[42] showed that 60 patients who underwent RPD exhibited significantly faster nutritional status recovery in terms of serum total protein and prealbumin as well as hemoglobin within 2 weeks after surgery compared with 120 patients who underwent OPD. They stated that this benefit might have resulted from earlier resumption of oral intake, less incisional pain, and a more relaxed psychological status, especially after parenteral nutrition was switched to enteral nutrition on postoperative day 5 to 7.[42] However, during the early postoperative phase (within 2 weeks), nutritional status indicators such as serum total protein, prealbumin, and hemoglobin can show high variability due to postoperative infection, intraoperative blood loss, use of perioperative blood transfusion and plasma fractionators, or morbidity. The abovementioned study by Chen et al[42] lacked a discussion of these points. In the present study, we analyzed nutritional and immunological indices in the postoperative medium-term period (4–8 weeks postoperatively) using cases in which textbook outcomes had been achieved to minimize the influence of infections, transfusion, or postoperative complications. Contrary to our hypothesis, the postoperative nutritional and immunological status indices (albumin, PNI, NLR, and PLR index) were equivalent between MIPD and OPD. To the best of our knowledge, this is the first study to compare the postoperative nutritional and immunological statuses of MIPD versus OPD in the postoperative medium-term period. From the study results, we inferred alternative therapeutic strategies to improve the nutritional and immunological statuses after PD. PD is accompanied by loss of pancreatic function and the need for gastrointestinal reconstruction, which results in pancreatic exocrine insufficiency and malnutrition. To recover the nutritional and immunological statuses as soon as possible postoperatively, comprehensive management and care such as gastrointestinal prokinetic agents, pancrelipase, or rehabilitation might be more important than the surgical approach.

Several limitations of this study should be considered. First, this was a single-center retrospective analysis and was therefore inherently susceptible to potential treatment selection bias and many unknown confounders. PSM was conducted to minimize the potential for selection bias and adjust for cofounders. A multicenter RCT is required to validate our findings. Second, our initial consecutive experience of MIPD and the learning curves for both LPD and RPD are underlying factors. Third, the timing of the first routine outpatient follow-up during which blood tests were performed to calculate the nutritional and immunological indices slightly differed among individual patients because of the retrospective nature of the study. The blood data were obtained at approximately 30 to 60 days postoperatively (median: 43 days, interquartile range: 39–50 days). In a future study, nutritional and immunological assessment using prospective data collection after PD may elucidate the true impact of MIPD on postoperative nutritional and immunological statuses.

CONCLUSIONS

MIPD for periampullary tumors may contribute to better surgical outcomes with less EBL, fewer intraoperative blood transfusions, shorter LOS, decreased postoperative complications (especially CR-POPF), and a higher achievement rate of textbook outcomes compared with OPD. The exception to these advantages is a prolonged operative time. MIPD and OPD were found to be comparable in terms of the number of dissected lymph nodes, R0 resection rate, and mortality rate. Taken together, these findings indicate that MIPD is a feasible procedure. However, despite these advantages of MIPD over OPD, no advantage with respect to the postoperative nutritional and immunological statuses was detectable even in the cohort that achieved textbook outcomes. Not only the surgical approach but also alternative therapeutic strategies such as comprehensive management and care to ameliorate pancreatic exocrine insufficiency or enhance rehabilitation may be important to improve the postoperative nutritional and immunological statuses after PD.

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REFERENCES

1. Jiang J, Upfill-Brown A, Dann AM, et al. Association of hospital length of stay and complications with readmission after open pancreaticoduodenectomy. *JAMA Surg*. 2019;154:88–90.
2. Yuan F, Essaji Y, Belley-Cote EP, et al. Postoperative complications in elderly patients following pancreaticoduodenectomy lead to increased postoperative mortality and costs. A retrospective cohort study. *Int J Surg*. 2018;60:204–209.
3. Zimmerman AM, Roye DG, Charpentier KP. A comparison of outcomes between open, laparoscopic and robotic pancreaticoduodenectomy. *HPB (Oxford)*. 2018;20:364–369.
4. Tran TB, Dua MM, Worhunsky DJ, et al. The first decade of laparoscopic pancreaticoduodenectomy in the United States: costs and outcomes using the Nationwide Inpatient Sample. *Surg Endosc*. 2016;30:1778–1783.
5. Adam MA, Choudhury K, Dinan MA, et al. Minimally invasive versus open pancreaticoduodenectomy for cancer: practice patterns and short-term outcomes among 7061 patients. *Ann Surg*. 2015;262:372–377.
6. Qin H, Qiu J, Zhao Y, et al. Does minimally-invasive pancreaticoduodenectomy have advantages over its open method? A meta-analysis of retrospective studies. *PLoS One*. 2014;9:e104274.
7. Ricci C, Casadei R, Taffurelli G, et al. Minimally invasive pancreaticoduodenectomy: what is the best "choice"? A systematic review and network meta-analysis of non-randomized comparative studies. *World J Surg*. 2018;42:788–805.
8. Nassour I, Wang SC, Christie A, et al. Minimally invasive versus open pancreaticoduodenectomy: a propensity-matched study from a national cohort of patients. *Ann Surg*. 2018;268:151–157.
9. Nassour I, Winters SB, Hoehn R, et al. Long-term oncologic outcomes of robotic and open pancreatectomy in a national cohort of pancreatic adenocarcinoma. *J Surg Oncol*. 2020;122:234–242.
10. Peng L, Lin S, Li Y, et al. Systematic review and meta-analysis of robotic versus open pancreaticoduodenectomy. *Surg Endosc*. 2017;31:3085–3097.
11. Zhou NX, Chen JZ, Liu Q, et al. Outcomes of pancreatoduodenectomy with robotic surgery versus open surgery. *Int J Med Robot*. 2011;7:131–137.
12. Palanivelu C, Senthilnathan P, Sabnis SC, et al. Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours. *Br J Surg*. 2017;104:1443–1450.

13. Poves I, Burdío F, Morató O, et al. Comparison of perioperative outcomes between laparoscopic and open approach for pancreatoduodenectomy: the PADULAP randomized controlled trial. *Ann Surg*. 2018;268:731–739.
14. Wang M, Li D, Chen R, et al; Minimally Invasive Treatment Group in the Pancreatic Disease Branch of China's International Exchange and Promotion Association for Medicine and Healthcare (MITG-P-CPAM). Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours: a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2021;6:438–447.
15. van Hilst J, de Rooij T, Bosscha K, et al; Dutch Pancreatic Cancer Group. Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial. *Lancet Gastroenterol Hepatol*. 2019;4:199–207.
16. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg*. 2009;250:187–196.
17. Bassi C, Marchegiani G, Dervenis C, et al; International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. *Surgery*. 2017;161:584–591.
18. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery*. 2007;142:20–25.
19. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery*. 2007;142:761–768.
20. Koch M, Garden OJ, Padbury R, et al. Bile leakage after hepatobiliary and pancreatic surgery: a definition and grading of severity by the International Study Group of Liver Surgery. *Surgery*. 2011;149:680–688.
21. Onodera T, Goseki N, Kosaki G. [Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients]. *Nihon Geka Gakkai Zasshi*. 1984;85:1001–1005.
22. van Roessel S, Mackay TM, van Dieren S, et al; Dutch Pancreatic Cancer Group. Textbook outcome: nationwide analysis of a novel quality measure in pancreatic surgery. *Ann Surg*. 2020;271:155–162.
23. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate Behav Res*. 2011;46:399–424.
24. Sattari SA, Sattari AR, Makary MA, et al. Laparoscopic versus open pancreatoduodenectomy in patients with periampullary tumors: a systematic review and meta-analysis. *Ann Surg*. 2023;277:742–755.
25. Sharpe SM, Talamonti MS, Wang CE, et al. Early national experience with laparoscopic pancreaticoduodenectomy for ductal adenocarcinoma: a comparison of laparoscopic pancreaticoduodenectomy and open pancreaticoduodenectomy from the National Cancer Data Base. *J Am Coll Surg*. 2015;221:175–184.
26. Klompmaker S, van Hilst J, Wellner UF, et al; European consortium on Minimally Invasive Pancreatic Surgery (E-MIPS). Outcomes after minimally-invasive versus open pancreatoduodenectomy: a Pan-European propensity score matched study. *Ann Surg*. 2020;271:356–363.
27. Croome KP, Farnell MB, Que FG, et al. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? *Ann Surg*. 2014;260:633–8; discussion 638.
28. Song KB, Kim SC, Hwang DW, et al. Matched case-control analysis comparing laparoscopic and open pylorus-preserving pancreaticoduodenectomy in patients with periampullary tumors. *Ann Surg*. 2015;262:146–155.
29. Kantor O, Pitt HA, Talamonti MS, et al. Minimally invasive pancreatoduodenectomy: is the incidence of clinically relevant postoperative pancreatic fistula comparable to that after open pancreatoduodenectomy? *Surgery*. 2018;163:587–593.
30. McMillan MT, Zureikat AH, Hogg ME, et al. A propensity score-matched analysis of robotic vs open pancreatoduodenectomy on incidence of pancreatic fistula. *JAMA Surg*. 2017;152:327–335.
31. Marjanovic G, Kuvendziska J, Holzner PA, et al. A prospective clinical study evaluating the development of bowel wall edema during laparoscopic and open visceral surgery. *J Gastrointest Surg*. 2014;18:2149–2154.
32. Kamarajah SK, Bundred J, Marc OS, et al. Robotic versus conventional laparoscopic pancreaticoduodenectomy a systematic review and meta-analysis. *Eur J Surg Oncol*. 2020;46:6–14.
33. Kim H, Choi SH, Jang JY, et al. Multicenter comparison of totally laparoscopic and totally robotic pancreaticoduodenectomy: propensity score and learning curve-matching analyses. *J Hepatobiliary Pancreat Sci*. 2022;29:311–321.
34. Wehrle CJ, Chang JH, Gross AR, et al. Comparing oncologic and surgical outcomes of robotic and laparoscopic pancreatoduodenectomy in patients with pancreatic cancer: a propensity-matched analysis. *Surg Endosc*. 2024;38:2602–2610.
35. Mazzola M, Giani A, Crippa J, et al. Totally laparoscopic versus open pancreaticoduodenectomy: a propensity score matching analysis of short-term outcomes. *Eur J Surg Oncol*. 2021;47(3 Pt B):674–680.
36. Vandeputte M, Vansteenkiste F, Ceelen W, et al. Morbidity and survival after laparoscopic versus open pancreatoduodenectomy: propensity score matched comparison. *Langenbecks Arch Surg*. 2023;408:16.
37. Stauffer JA, Coppola A, Villacreses D, et al. Laparoscopic versus open pancreaticoduodenectomy for pancreatic adenocarcinoma: long-term results at a single institution. *Surg Endosc*. 2017;31:2233–2241.
38. de Rooij T, van Hilst J, Topal B, et al; Dutch Pancreatic Cancer Group. Outcomes of a multicenter training program in laparoscopic pancreatoduodenectomy (LAELAPS-2). *Ann Surg*. 2019;269:344–350.
39. Wu Y, Peng B, Liu J, et al; Minimally Invasive Treatment Group in the Pancreatic DiseaseBranch of China's International Exchange and Promotion Association for Medicine and Healthcare (MITG-P-CPAM). Textbook outcome as a composite outcome measure in laparoscopic pancreaticoduodenectomy: a multicenter retrospective cohort study. *Int J Surg*. 2023;109:374–382.
40. Nickel F, Wise PA, Müller PC, et al. Short-term outcomes of robotic versus open pancreatoduodenectomy: propensity score-matched analysis. *Ann Surg*. 2024;279:665–670.
41. Nicholas E, van Roessel S, de Burlet K, et al. Using textbook outcomes to benchmark practice in pancreatic surgery. *ANZ J Surg*. 2021;91:361–366.
42. Chen S, Chen JZ, Zhan Q, et al. Robot-assisted laparoscopic versus open pancreaticoduodenectomy: a prospective, matched, mid-term follow-up study. *Surg Endosc*. 2015;29:3698–3711.