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Outcomes after minimally invasive versus open total pancreatectomy: a pan-European propensity score matched study

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MINI-ABSTRACT (36/50)

This pan-European multicenter propensity score matched study found, among selected patients, a lower 90-day postoperative major morbidity after minimally invasive total pancreatectomy (MITP) as compared to open total pancreatectomy (OTP) with similar 90-day mortality and survival.

ABSTRACT

Objective: To assess postoperative 90-day outcomes after minimally invasive (laparoscopic/robot-assisted) total pancreatectomy (MITP) in selected patients versus open total pancreatectomy (OTP) among European centers.

Background: Minimally invasive pancreatic surgery is becoming increasingly popular but data on MITP are scarce and multicenter studies comparing outcomes versus OTP are lacking. It therefore remains unclear if MITP is a valid alternative.

Methods: Multicenter retrospective propensity-score matched study including consecutive adult patients undergoing MITP or OTP for all indications at 16 European centers in 7 countries (2008-2017). Patients after MITP were matched (1:1, caliper 0.02) to OTP controls. Missing data were imputed. The primary outcome was 90-day major morbidity (Clavien-Dindo ≥3a). Secondary outcomes included 90-day mortality, length of hospital stay, and survival.

Results: Of 361 patients (99 MITP/262 OTP), 70 MITP procedures (50 laparoscopic, 15 robotic, 5 hybrid) could be matched to 70 OTP controls. After matching, MITP was associated with a lower rate of major morbidity (17% MITP vs 31% OTP, P = 0.022). The 90-day mortality (1.4% MITP vs 7.1% OTP, P = 0.209) and median hospital stay (17 [IQR 11-24] MITP vs 12 [10-23] days OTP, P = 0.876) did not differ significantly. Among 81 patients with PDAC, overall survival was 3.7 (IQR 1.7-N/A) vs 0.9 (IQR 0.5-N/A) years, for MITP vs OTP, which was non-significant after stratification by T-stage.

Conclusion: This international propensity score matched study showed that MITP may be a valuable alternative to OTP in selected patients, given the associated lower rate of major morbidity.

INTRODUCTION

Total pancreatectomy is gaining popularity resulting from increased comprehension of main duct intraductal papillary mucinous neoplasm (IPMN), improved neoadjuvant treatment regimens (e.g. FOLFIRINOX) for pancreatic cancer, and improved treatment options for exocrine and endocrine insufficiency.[1,2]

Minimally invasive total pancreatectomy (MITP), which includes laparoscopic and robotic surgery, aims to reduce the treatment burden compared to open total pancreatectomy (OTP).[3,4] To date, only nine studies have reported on clinical outcomes after MITP, including a total of 47 patients. These studies have suggested that, albeit technically more demanding than OTP, MITP is feasible and safe in well-selected patients, with acceptable morbidity (19%) and mortality (0%) rates.[4–11] However, none of these studies used case-matching to mitigate the effects of confounding (e.g. surgical case selection) between MITP and OTP.[12] Further, the single-center nature of most studies limits their external validity. This lack of evidence is the main reason that MITP was not addressed in the recent Miami international evidence-based guidelines for minimally invasive pancreatic resection.[13]

The purpose of this study was to compare surgical, oncological, and functional 90-day outcomes after MITP versus OTP among European centers. We hypothesized that MITP is associated with equivalent major morbidity and superior secondary outcomes (mortality, length of hospital stay) compared to OTP.

METHODS

A propensity score matched study was performed, comparing MITP to OTP controls, in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[14] A predefined study protocol was made available online and approved by the Scientific and Research Committee of the European-African Hepato-Pancreato-Biliary Association (E-AHPBA) as well as by the senior co-authors.[15] The need for patient informed consent was waived by the medical ethics committee at the Amsterdam UMC, location Academic Medical Center.

Eligibility and data collection

Surgeons were invited to participate through three e-mail notifications via the European consortium on Minimally Invasive Pancreatic Surgery (E-MIPS), which includes over 80 centers. Interested centers received a survey (Google™ Survey, Mountain View, CA, USA), regarding annual MITP and OTP volumes and practice standards. After they confirmed their participation, patient data were pseudonymously collected via a GDPR- and HIPAA-compliant on-line electronic case report form (eCRF) and data storage environment (CASTOR®, CIWIT B.V., Amsterdam). Data collection was monitored and supervised by the study coordinators (LS, SK). All indications for MITP or OTP were included; pancreatic-, bile duct-, or duodenal cancer, IPMN, pNET, chronic pancreatitis (with the exclusion of autologous islet transplantation), or other. We also included patients with an intra-operative decision to perform a TP (completion TP), and these patients were matched to similar OTP procedures. All OTP procedures came from centers that performed MITP. All consecutive patients undergoing elective MITP (laparoscopic or laparoscopic with open anastomosis [hybrid], robot-assisted), or OTP were included from the participating centers, between January 1st, 2008 and December 31st, 2017. Patients were analyzed according to the intended approach, regardless of conversion to open surgery.

Primary and secondary outcomes

The primary outcome was 90-day major morbidity, defined as Clavien-Dindo ≥3a complications.[16] Secondary outcomes were 90-day mortality, length of hospital stay, estimated operative blood loss (EBL), operative time, conversion to OTP, resection margin status (R0/R1/R2, described below),[17] malignant lymph node ratio, and overall survival. Endo- and exocrine insufficiency outcomes were use of insulin-injections or insulin-pump, HbA1c level after 3 months, and dose and frequency of pancreatic enzymes.

Definitions

Preoperative variables were baseline characteristics: age, sex, body-mass-index (BMI), and comorbidities (Charlson comorbidity index[18]), surgical history, CT/MRI-scan information (vascular/organ involvement), American Society of Anesthesiologists (ASA) classification[19], and Eastern Cooperative Oncology Group (ECOG) performance status.

Conversion was recorded if a laparoscopic or robotic MIPD was converted to OPD.[20] Postoperative complications were captured and classified according to the Clavien-Dindo classification of surgical complications.[16] The definitions of the International Study Group on Pancreatic Surgery (ISGPS) and International Study Group of Liver Surgery (ISGLS) were used to classify delayed gastric emptying[21], post pancreatectomy hemorrhage (PPH), and bile leakage grade B/C. [22] Surgical site infections were defined using the Center for Disease Control and Prevention (CDC) definition.[23] Resection margins were categorized according to the Royal College of Pathologists[17] definition and classified into R0 (distance margin to tumor ≥ 1mm), R1 (distance margin to tumor < 1mm) and R2 (macroscopically positive margin). Length of hospital stay was defined as days between operation and date of discharge. Diabetes mellitus (DM) was defined as the need for anti-diabetic medication and new-onset diabetes mellitus (NODM) as newly diagnosed DM within one year after operation. Exocrine insufficiency was defined as the need for pancreatic enzyme supplementation.

Propensity score matching

MITP and OTP controls were matched using propensity scores following the recommendations by Lonjon et al.[24] Matching was done on a 1:1 ratio without replacement, with a standard caliper width of 0.02 of the standard deviation of the log propensity score. Propensity scores were determined based on logistic regression including the following covariates: year of surgery, geographical region, setting (primary TP vs completion or converted), sex, age, ASA-classification, BMI, prior abdominopelvic surgery, Charlson comorbidity index, preoperative diagnosis, and preoperative tumor diameter (CT-scan). The matching per geographical region was based on socio-economic and cultural similarities (e.g. discharge policy) and consisted of the following groups: Germany-Netherlands; France; Spain-Italy; Turkey-Russia. Matching could not be performed on country level due to the limited number of patients included in the study.

Statistical analyses

Data were analyzed using STATA version 14.1 (StataCorp LP, College Station, Texas, US). The standardized mean difference (SMD) was used to assess balance at baseline in both groups. The student's t, Mann Whitney U, Chi-square, or Fisher's exact tests were used as appropriate to compare outcomes between groups. Kaplan-Meier survival curves and the Log-Rank test were used to compare survival. Alpha <0.05 was used to indicate statistical significance. Missing data were resolved by multiple chained imputation (MICE) wherever appropriate. All analyses were performed based on modified intention to treat (i.e. intended surgical approach). Categorical data are presented as proportions, continuous data as either mean and standard deviation (SD) or median and inter-quartile-range (IQR) as appropriate. Subgroup analyses were performed to assess possible differences between geographical regions. Assessing differences between laparoscopic, robot-assisted, and hybrid MITP was forgone because of the small number of robotic (15) and hybrid (5) procedures.

RESULTS

Among 16 participating centers, data from 463 patients were retrieved. After exclusions, 99 MITP and 262 OTP patients remained in the study. After propensity score matching, 70 patients were included in each group (Fig. 1). Participating centers had a median annual TP volume of 5 (IQR 2-12) and all performed MITP. The median annual case-volume was 2 (IQR 1-4) for MITP and 3 (IQR 1-13) for OTP. The median follow-up time was 1.0 year (IQR 0.5-2.4) for MITP and 0.8 year (0.3-3.0) for OTP.

Selection criteria for MITP

All 16 centers reported their selection criteria for MITP. Absence of vascular involvement (7 out of 16 centers) was the most frequent criterion, followed by BMI ≤35 kg/m2 (2 out of 16), and absence of previous abdominal surgery (2 out of 16). All reported selection criteria are presented in Figure 2.

Baseline characteristics

Baseline characteristics before and after matching are presented in Table 1. After propensity score matching, groups were well balanced although some minor, clinically irrelevant, differences remained; The MITP group had slightly larger tumors (28mm vs 25mm; SMD 0.20) and fewer PNETs (4.3% vs 8.6%; SMD -0.20). The balance in geographical regions also improved after matching, but centers from Germany and the Netherlands (DE-NL) were slightly overrepresented in the MITP group compared to the OTP group (16% of all MITP vs 7.1% of all OTP procedures; SMD 0.27).

Primary and secondary outcomes

After matching, the 90-day major morbidity rate was lower after MITP; 12 (17%) MITP versus 22 (31%) OTP (P = 0.020). After imputation for missing data (n=6), this difference remained statistically significant (17% vs 33%, P = 0.036). The 90-day mortality rate did not differ significantly (1.4% vs 7.1%, P = 0.209), for MITP vs OTP, respectively. In the MITP group, one patient died of a Grade C PPH 30 days after surgery. In the OTP group, causes of death were septic shock of unknown cause (2), grade B PPH (1), myocardial infarction (1), progressive disease (1).

Median operative time was longer in the MITP group (475 vs 377 minutes, P <0.001). The rates of additional organ resections were similar (56% vs 54%, P > 0.99). In the minimally invasive group, conversion to open surgery was recorded in 21 of 50 (42%) laparoscopic and 2 of 15 (13.3%) robotic procedures. Median length of hospital stay was longer in the MITP group (17 [IQR 11-24] vs 12 [IQR 10-23] days), but this was not statistically significant (mean 19 vs 19 days, P = 0.876). See Table 2 for all secondary outcomes.

Oncologic outcomes before and after matching are presented in Table 3. Outcomes were comparable between groups, but the MITP group had significantly more resections with N0-status (57% vs 34%; P = 0.011). The total number of lymph nodes retrieved was not statistically different (22% vs 24%; P = 0.154). For the 81 patients with PDAC, the median overall survival was 3.7 years (IQR 1.7-N/A) for MITP and 0.9 years (IQR 0.5-N/A) for OTP. Of note, the upper confidence levels could not be determined due to the limited number of deaths within the study follow-up time. Supplement 1, http://links.lww.com/SLA/D272 shows the observed survival curves for PDAC, stratified by histological T-stage. There was no significant difference between MITP vs OTP in both the Tis-T2 (P = 0.209) and T3-T4 strata (P = 0.082).

Table 4 shows the functional outcomes. Diabetic status was missing in 8 and 6 patients after MITP and OTP, respectively. Of all patients with new-onset diabetes, 43 out of 45 in the MITP group vs 40 out of 43 patients in the OTP group were treated with insulin injections (P = 0.731). The other patients in both groups were treated with insulin pumps. Only 5 of 88 patients with new-onset diabetes had an insulin pump. As expected, the median HbA1c level at three months was comparable between MITP and OTP (54 mmol/mol vs 58 mmol/mol, P = 0.086) as was the use of pancreatic enzymes (86% vs 87%, P > 0.99).

Sensitivity analyses

In an analysis per geographical region, lengths of stay did not significantly differ between MITP and OTP. In an unadjusted post-hoc analysis, pre-existing diabetes was associated with prolonged hospital stay after MITP (median 17 vs 13 days, p= 0.022), but no differences were seen after OTP (median 15 vs 15 days, p=0.22). The main study results remained similar in a sensitivity analysis that excluded all hybrid and robotic procedures, see Supplement 5, http://links.lww.com/SLA/D277. The rate of major morbidity in laparoscopic TP (without hybrid and robotic cases) was 20.0% vs 31.0% in OTP, P = 0.141 (P = 0.119 after imputation). The lack of significance in this sensitivity analysis may be due to power loss as a result of the reduced MITP group size. Of note, 1 out of 5 (1 missing outcome) and 1 out of 15 patients had a major complication after hybrid and robotic TP, respectively (p = 0.382 after imputation).

DISCUSSION

This first international multicenter propensity score matched study found that MITP was associated with 14% fewer major complications compared to OTP, among selected patients. Length of stay, 90-day mortality, functional outcomes, and survival were comparable.

The current findings can only be compared to earlier monocenter studies due to a lack of multicenter studies. A case-matched analysis comparing 11 patients after MITP with 11 patients after OTP, reported a 500 mL lower mean intraoperative blood loss, faster recovery of patient mobility, passage of first flatus, first bowel movement, full oral diet intake, lower pain scores, and a decreased need for analgesics on postoperative day 1 and 3 in favor of MITP.[12] In the current study overall major morbidity was 14% lower in the MITP group, including fewer non-surgical interventions (8.6% vs. 12.9%), fewer reoperations (2.9% vs. 8.6%), and fewer deaths (1.4% vs. 7.1%). The intraoperative blood loss was similar, (MITP 379ml vs. OTP 367ml). Giulianotti and Wang *et al.* found that blood loss was 266ml (range 100-400), 310ml (range 50-650) respectively in MITP.[3,11]

Other studies reported higher median blood loss after MITP.[4–7] In the current multicenter study the mean operative time was 100 minutes longer after MITP. Boggi *et al.* found a longer mean length of hospital stay after MITP (27 days (12-88) vs. 17 days (12-34)). In the current study, the median length of hospital stay was also longer in the MITP group (17 [IQR 11-24] vs 12 [IQR 10-23] days), but this was not statistically significant (mean 19 vs 19 days, P = 0.876).

For pancreatoduodenectomy, it remains unclear whether the minimally invasive approach leads to reduced overall morbidity and time to functional recovery or hospital stay, as the three available randomized trials show conflicting results.[25–27] Some argue that increased fistula rates after MIPD compared to ODP offset the benefits of the minimally invasive approach.[28] However, in a meta-analysis of the three randomized trials the rate of pancreatic fistula did not differ between laparoscopic and open pancreatoduodenectomy.[29] The fact that MITP does not require a pancreatic anastomosis probably explains the lower rate of major morbidity after MITP found in the current study.

Minimally invasive distal pancreatectomy (MIDP) may indeed also be associated with lower major morbidity.[30,31] Although the recent first two randomized trials (LEOPARD and LAPOP) could not confirm this hypothesis, both studies were only powered to detect a difference in time to functional recovery.[32,33] However, a recent international multicenter study did report a 11% reduction in major morbidity after MIDP as compared to ODP.[34] On the other hand, although MIDP leads to shorter time to functional recovery and shorter hospital stay compared to open distal pancreatectomy[30], such an effect appears absent in MITP. The need for advanced diabetes care after total pancreatectomy may mitigate the effect of MITP in terms of hospital stay. It remains speculative, but advancement through the collective learning curve might improve overall outcomes after MITP in the (near) future.

This study has some limitations. First, although we applied propensity score matching, we could not adjust for unmeasured and/or unknown confounders. This may have caused residual imbalance between treatment groups. Nevertheless, we think most important clinically relevant confounders were included. Second, accurate ascertainment of baseline- and outcome variables may have been affected by between-center differences in data collection and reporting, surgical case selection, local protocols, and postoperative management. The impact on comparing MITP to OTP is probably minimal as geographical regions were evenly distributed between the two groups. Third, ascertainment of outcomes was based on return hospital visits, limiting the available follow-up times. As a result, the upper survival interquartile-range could not be established. Nevertheless, median overall survival after MITP doesn't appear to differ from OTP. Fourth, because of the limited sample size, no subgroup analysis could be performed on laparoscopic- vs robotic- vs hybrid MITP. A sensitivity analysis that excluded all hybrid and robotic procedures found similar lengths of stay between MITP and OTP although this difference was not significant anymore. Fifth, quality of life could not be compared between groups in this retrospective study and remains to be studied in order to adequately counsel patients for either procedure.

Strengths of this study include its international multicenter design with propensity score matching. Its internal validity is strengthened by a predefined study protocol that was approved by all centers prior to the study. Inclusion criteria, center characteristics, and patient selection criteria were clearly defined which improves the external validity. Furthermore, the risk of reporting bias was reduced by offering anonymity to participating centers and commitment to the predefined study protocol. Topics for further study are quality of life after MITP vs OTP, the impact of annual procedure volumes and learning curve, and the effect of novel endocrine and exocrine treatment on functional outcomes.

In conclusion, this study found that, in selected patients, MITP was associated with a 14% lower major morbidity rate, without statistically significant differences in 90-day mortality rate, length of hospital stay, functional outcome, and overall survival, as compared to OTP.

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SUPPLEMENT 2A: http://links.lww.com/SLA/D273.

SUPPLEMENT 2B: http://links.lww.com/SLA/D274.

SUPPLEMENT 3: http://links.lww.com/SLA/D275.

SUPPLEMENT 4: http://links.lww.com/SLA/D276.

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FIGURE AND TABLE LEGEND

FIGURE 1. Study Flow-chart

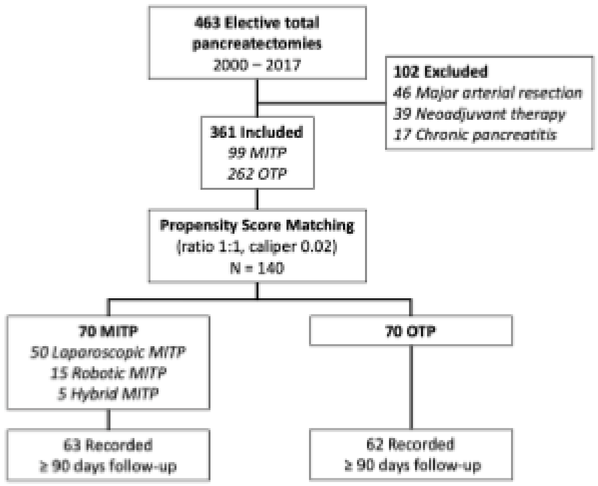
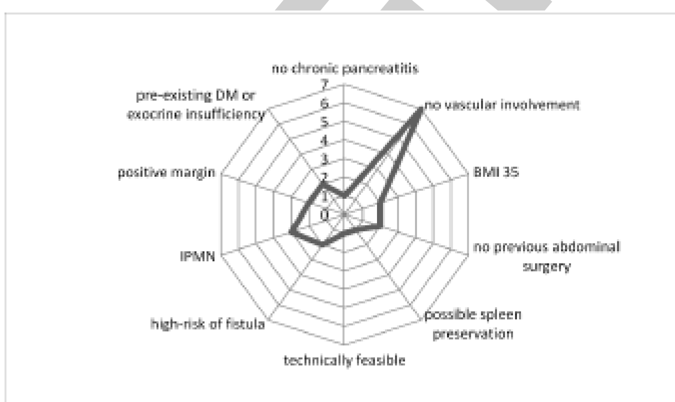


FIGURE 2. Selection criteria for MITP.



BMI, body mass index; IPMN, intraductal papillary mucinous neoplasm; DM, diabetes mellitus.

TABLE 1. Baseline characteristics of the unmatched and matched cohorts

Baseline	**OTP Before Matching n=262**		**OTP After Matching n=70**		**MITP After Matching n=70**		**SMD Before**	**SMD After**
Age, mean (SD), y	69	(25.7)	66	(12.4)	68	(8.9)	-0.09	0.08
Median (IQR)	69	(61-76)	68	(58-77)	69	(63-74)		
Female sex, No. (%)	117	(44.7)	31	(44.3)	30	(42.9)	-0.02	-0.03
BMI, mean (SD), y	25	(4.0)	25	(3.7)	25	(3.5)	0.02	0.03
Median (IQR)	25	(22-27)	25	(22-27)	24	(22-26)		
Diabetes Mellitus, No. (%)	90	(34.4)	21	(30.0)	22	(31.4)	0	0.03
Charlson CI, mean (SD)	1	(1.1)	1	(0.9)	1	(1.2)	-0.07	0.09
ASA Physical Status, No. (%)								
ASA-1	17	(6.5)	7	(10.0)	5	(7.1)	0.02	-0.11
ASA-2	126	(48.1)	25	(35.7)	26	(37.1)	-0.15	0.03
ASA-3/4	114	(43.5)	36	(51.4)	38	(54.3)	0.16	0.06
ASA Unknown	5	(1.9)	2	(2.9)	1	(1.4)	-0.07	-0.12
Abdominopelvic surgical history	126	(49.4)	27	(40.9)	29	(43.3)	-0.14	0.05
Preoperative CT-imaging								
Tumor diameter, mean (SD), mm	32	(18.4)	25	(15.4)	28	(12.4)	-0.3	0.20
Median (IQR)	30	(20-39)	22	(14-30)	27	(20-35)		
Preoperative diagnosis, No. (%)								

PDAC	153	(58.4)	37	(52.9)	37	(52.9)	-0.26	0
PNET	14	(5.3)	6	(8.6)	3	(4.3)	-0.06	-0.20
IPMN/MCN	57	(21.8)	22	(31.4)	23	(32.9)	0.45	0.03
Other Adenocarcinoma*	24	(9.2)	3	(4.3)	6	(8.6)	-0.12	0.16
Other	12	(4.6)	2	(2.9)		(.)	-0.22	-0.17
Geographical region, No. (%)								
DE-NL	32	(12.2)	5	(7.1)	11	(15.7)	-0.03	0.27
ES-IT	196	(74.8)	40	(57.1)	35	(50.0)	-0.81	-0.15
FR	16	(6.1)	11	(15.7)	11	(15.7)	0.42	0
RUS-TR	18	(6.9)	14	(20.0)	13	(18.6)	0.65	-0.04

CAPTION: Preoperative patient characteristics. Propensity score matching (caliper 0.02) variables: year of surgery, geographical region (DE-NL vs FR vs ES-IT vs TR-RUS), setting (primary TP vs completion or converted), sex, age, ASA-classification, BMI, prior abdominopelvic surgery, Charlson comorbidity index, preoperative diagnosis, preoperative tumor diameter (CT-scan). * Includes any adenocarcinoma type (e.g. cholangiocarcinoma). Abbreviations: OTP, open total pancreatectomy; MITP, minimally invasive total pancreatectomy; ASA, American Society for Anesthesiologists (classification); IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuro-endocrine tumor; SMD, standardized mean difference; DE, Germany; NL, the Netherlands; ES, Spain; IT, Italy; FR, France; RUS, Russia; TR, Turkey

TABLE 2. Intraoperative and 90-day outcomes after MITP vs OTP

Perioperative	**OTP Before Matching n=262**		**OTP After Matching n=70**		**MITP After Matching n=70**		**P-Value***
Operative time, mean (SD), min.	413	(116.8)	377	(92.6)	475	(120.2)	<0.001
Median (IQR)	393	(335-469)	361	(316-440)	480	(385-548)	
Blood loss, mean (SD, ml.	388	(402.5)	367	(223.7)	379	(328.9)	0.81
Median (IQR)	300	(200-415)	300	(200-450)	300	(150-490)	
Type of procedure, No. (%)							
Primary elective TP	113	(43.1)	40	(57.1)	37	(52.9)	0.734
Completion elective TP	22	(8.4)	7	(10.0)	7	(10.0)	>0.99
Intraoperative conversion to TP	127	(48.5)	23	(32.9)	26	(37.1)	0.723
Additional organs resected, No. (%)	110	(42.1)	38	(54.3)	39	(55.7)	>0.99
Splenectomy	102	(38.9)	36	(51.4)	36	(51.4)	>0.99
Gastrectomy	8	(3.1)	3	(4.3)	8	(11.4)	0.208
Venous resection, No. (%)	76	(29.0)	18	(25.7)	13	(19.1)	0.417
Pancreatic texture, No. (%)							
Hard/firm pancreas	117	(44.7)	31	(44.3)	23	(32.9)	0.224
Aspect unknown	14	(5.3)	6	(8.6)	9	(12.9)	
90-Day Postoperative							
Length of Stay, mean (SD), d	21	(23.9)	19	(13.2)	19	(11.8)	0.876
Median (IQR)	15	(12-23)	12	(10-23)	17	(11-24)	

Morbidity, No. (%)							
No complications	110	(42.0)	33	(47.1)	38	(54.3)	0.499
Grade 1-2 (minor)	69	(26.3)	10	(14.3)	19	(27.1)	0.094
Grade 3a (non-surgical intervention)	17	(6.5)	9	(12.9)	6	(8.6)	0.586
Grade 3b (reoperation)	17	(6.5)	6	(8.6)	2	(2.9)	0.275
Grade 4a-4b (major)	7	(2.7)	2	(2.9)	3	(4.3)	>0.99
Grade 5 (death)	36	(13.7)	5	(7.1)	1	(1.4)	0.209
Bile leakage grade B/C, No. (%)	10	(3.9)	4	(6.2)	1	(1.5)	0.205
Hemorrhage grade B/C, No. (%)	30	(11.8)	5	(7.7)	6	(8.7)	>0.99
Del. gast. emptying grade B/C, No. (%)	17	(6.7)	2	(3.1)	1	(1.4)	0.608
Non-pancreatic complications+, No (%)	72	(28.1)	17	(26.2)	11	(15.9)	0.202
Readmission within 90 days, No (5)	14	(6.1)	4	(6.5)	6	(9.4)	0.744
Readmission LOS, mean (SD), d	12	(13.6)	6	(4.5)	13	(10.9)	0.232
Median (IQR)	5	(5-12)	4	(3-9)	11	(5-15)	

CAPTION: * Significance test after matching. + Includes: abdominal surgical site infection, septic shock, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, pulmonary embolism, or stroke. Abbreviations: OTP, open total pancteatectomy; MITP, minimally invasive total pancreatectomy; LOS, length of stay; IQR, interquartile range; SD, standard deviation

TABLE 3. Pathology and oncologic outcomes after MITP vs OTP

Pathology	OTP Before Matching n=262		OTP After Matching n=70		MITP After Matching n=70		P-Value
Histology, No. (%)							
PDAC	152	(58.0)	41	(58.6)	40	(57.1)	>0.99
Tis-T2	36	(13.7)	13	(18.6)	15	(21.4)	0.833
T3-T4	115	(43.9)	27	(38.6)	25	(35.7)	0.861
Other Adenocarcinoma*	25	(9.5)	4	(5.7)	4	(5.7)	>0.99
PNET	14	(5.3)	6	(8.6)	3	(4.3)	0.493
IPMN/MCN	45	(17.2)	15	(21.4)	17	(24.3)	0.841
Low-intermediate	12	(4.6)	4	(5.7)	10	(14.3)	0.157
High-grade/Invasive	26	(9.9)	8	(11.4)	5	(7.1)	0.562
Other	25	(9.5)	3	(4.3)	5	(7.1)	0.718
Unknown	1	(0.4)	1	(1.4)	1	(1.4)	
Differentiation, No. (%)							
Grade ≤3	154	(58.8)	35	(50.0)	34	(48.6)	>0.99
Unknown	56	(21.4)	25	(35.7)	22	(31.4)	
Tumor diameter, mean (SD), mm	32	(18.0)	29	(18.9)	29	(16.3)	0.991
Median (IQR)	30	(20-40)	25	(20-35)	30	(21-39)	
Margin status, No. (%)							
R0	152	(58.0)	46	(65.7)	54	(77.1)	0.190
Unknown	19	(7.3)	7	(10.0)	8	(11.4)	
Nodal status, No. (%)							
N0	101	(38.5)	24	(34.3)	40	(57.1)	0.011
Unknown	11	(4.2)	7	(10.0)	4	(5.7)	
Total node harvest, mean (SD), n	41	(23.0)	37	(23.8)	31	(21.7)	0.154
Median (IQR)	38	(22-55)	35	(18-51)	24	(18-33)	
Metastasis, No. (%)							

M0	238	(90.8)	61	(87.1)	68	(97.1)	0.055
Unknown	7	(2.7)	2	(2.9)	1	(1.4)	
Adjuvant therapy, No. (%)							
None	134	(51.1)	37	(52.9)	37	(52.9)	>0.99
Chemoradiation	22	(8.4)	3	(4.3)	4	(5.7)	>0.99
Chemotherapy	77	(29.4)	22	(31.4)	23	(32.9)	>0.99
Unknown	29	(11.1)	8	(11.4)	6	(8.6)	

CAPTION: * Includes any adenocarcinoma type (e.g. cholangiocarcinoma). Abbreviations: OTP, open total pancreatectomy; MITP, minimally invasive total pancreatectomy; PDAC, pancreatic ductal adenocarcinoma; PNET, pancreatic neuro-endocrine tumor; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; IQR, interquartile range; SD standard deviation**.**

TABLE 4. Functional outcomes after MITP vs OTP

Endocrine function	**OTP Before Matching n=262**		**OTP After Matching n=70**		**MITP After Matching n=70**		**P-Value**
Diabetes Mellitus, No. (%)							
New-onset DM	163	(62.2)	43	(61.4)	45	(64.3)	0.861
Insulin injections	168	(64.1)	40	(57.1)	43	(61.4)	0.731
Insulin pump	4	(1.5)	3	(4.3)	2	(2.9)	>0.99
Unknown	1	(0.4)	-		-		-
Worsened DM	32	(12.2)	10	(14.3)	9	(12.9)	>0.99
Unchanged	56	(21.4)	11	(15.7)	8	(11.4)	0.623
Unknown	11	(4.2)	6	(8.6)	8	(11.4)	0.779
HbA1c (3 months), mean (SD), mmol/mol	57	(19.9)	53	(24.1)	43	(26.0)	0.086
Median (IQR)	59	(52-68)	58	(50-64)	54	(12-60)	
Unknown	125	(47.7)	34	(48.6)	35	(50.0)	
Exocrine function							
Exocrine insufficiency, No. (%)	232	(88.5)	61	(87.1)	60	(85.7)	>0.99
Unknown	17	(6.5)	7	(10.0)	9	(12.9)	

CAPTION: Abbreviations: OTP, open total pancreatectomy; MITP, minimally invasive total pancreatectomy; DM, diabetes mellitus; SD, standard deviation; IQR, interquartile range.