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Robot-assisted versus laparoscopic pancreatoduodenectomy: a pan-European multicenter propensity-matched study

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ABSTRACT

Background: The use of robot-assisted and laparoscopic pancreatoduodenectomy is increasing, yet large adjusted analyses that can be generalized internationally are lacking. This study aimed to compare outcomes after robot-assisted pancreatoduodenectomy and laparoscopic pancreatoduodenectomy in a pan-European cohort.

Methods: An international multicenter retrospective study including patients after robot-assisted pancreatoduodenectomy and laparoscopic pancreatoduodenectomy from 50 centers in 12 European countries (2009–2020). Propensity score matching was performed in a 1:1 ratio. The primary outcome was major morbidity (Clavien–Dindo ≥III).

Results: Among 2,082 patients undergoing minimally invasive pancreatoduodenectomy, 1,006 underwent robot-assisted pancreatoduodenectomy and 1,076 laparoscopic pancreatoduodenectomy. After matching 812 versus 812 patients, the rates of major morbidity (31.9% vs 29.6%; $P = .347$) and 30-day/in-hospital mortality (4.3% vs 4.6%; $P = .904$) did not differ significantly between robot-assisted pancreatoduodenectomy and laparoscopic pancreatoduodenectomy, respectively. Robot-assisted pancreatoduodenectomy was associated with a lower conversion rate (6.7% vs 18.0%; $P < .001$) and higher lymph node retrieval (16 vs 14; $P = .003$). Laparoscopic pancreatoduodenectomy was associated with shorter operation time (446 minutes versus 400 minutes; $P < .001$), and lower rates of postoperative pancreatic fistula grade B/C (19.0% vs 11.7%; $P < .001$), delayed gastric emptying grade B/C (21.4% vs 7.4%; $P < .001$), and a higher R0-resection rate (73.2% vs 84.4%; $P < .001$).

Conclusion: This European multicenter study found no differences in overall major morbidity and 30-day/in-hospital mortality after robot-assisted pancreatoduodenectomy compared with laparoscopic pancreatoduodenectomy. Further, laparoscopic pancreatoduodenectomy was associated with a lower rate of postoperative pancreatic fistula, delayed gastric emptying, wound infection, shorter length of stay, and a higher R0 resection rate than robot-assisted pancreatoduodenectomy. In contrast, robot-assisted pancreatoduodenectomy was associated with a lower conversion rate and a higher number of retrieved lymph nodes as compared with laparoscopic pancreatoduodenectomy.

Introduction

Pancreatoduodenectomy (PD) is used for the treatment of pancreatic head and periampullary tumors and is associated with relatively high postoperative morbidity and mortality.[1] Minimally invasive PD (MIPD) has gained wider acceptance over the last decade. The first reported laparoscopic PD (LPD) was in 1994.[2] Almost 10 years later, in 2003, the first robot-assisted PD (RPD) was reported.[3] Both RPD and LPD are challenging procedures requiring advanced skills for both the resection and the reconstruction phases.[4] The robotic approach appears to offer some surgical advantages compared to the laparoscopic approach due to wristed instruments, three-dimensional vision, which is console surgeon controlled, stabilized and scaled movement, additional control of a third and fourth arm control by the primary surgeon, and improved ergonomics.[5-8] Those advantages may be less evident for highly skilled laparoscopic surgeons but can be very helpful for surgeons. Nevertheless, RPD is associated with higher costs.[9-11]

In the past six years, four randomized trials have compared laparoscopic- and open pancreatoduodenectomy.[12-15] Three trials from India, Spain, and China showed beneficial outcomes of LPD, mostly shorter hospital stay,[12,13,15] whereas the Dutch multicenter LEOPARD-2 trial was stopped early due to safety concerns.[14] As a result, in several countries, the use of RPD increased, whereas the use of LPD decreased.[16,17]

Current studies comparing RPD and LPD are mostly retrospective and single-center, therefore, they are not representable for general practice.[18,19] Large, international multicenter comparative studies on RPD versus LPD, using propensity score matching (PSM), have not been performed. Therefore, this study aimed to compare RPD versus LPD using PSM in a large multicenter European cohort.

Materials and Methods

This study was initiated and performed by the European Consortium on Minimally Invasive Pancreatic Surgery (E-MIPS), and data were extracted from the retrospectively collected database. Outcomes were analyzed in the matched and non-matched cohorts.

Eligibility and Data Collection

Patients undergoing RPD and LPD for all indications were included from 50 centers in 12 European countries (2009–2020). Data were collected retrospectively through an International Conference on Harmonization Good Clinical Practice compliant online electronic case report form and data storage environment (CASTOR, CIWIT B.V., Amsterdam, the Netherlands). Data collection was limited to in-hospital or (in case of earlier discharge) 30-day outcomes. All hybrid and open procedures and procedures other than PD were excluded. Hybrid was defined as requiring incisions other than the extraction site. We did not classify open anastomosis through the extraction site as a hybrid procedure. Patients whose procedure/approach was unknown or whose primary outcome was missing were also excluded. In the case of conversion (ie, from a minimally invasive to an open approach), patients were included in the minimally invasive group.

Patient Selection

Indications for minimally invasive pancreatoduodenectomy varied between centers but generally included the absence of (or very limited) portomesenteric vein or arterial involvement and a body mass index (BMI) <35 kg/m^2.

Outcomes and Definitions

Baseline characteristics included age; BMI; sex; American Society of Anesthesiologists physical status classification system (ASA); comorbidities; preoperative abdominal surgery; perioperative use of somatostatin analogs; the presence of preoperative duct dilation (diameter >5 mm); vascular and organ involvement, neoadjuvant therapy; tumor size, and histopathologic determined malignancy. Intraoperative characteristics included operative time, estimated intraoperative blood loss, and type of resection (conversion and multivisceral). Postoperative outcomes included: major morbidity (Clavien–Dindo ≥III);[20] wound infection; postoperative pancreatic fistula (POPF);[21] postpancreatectomy hemorrhage (PPH)[1]; delayed gastric emptying (DGE)[22]; bile leakage[23]; 30-day/in-hospital mortality; reoperation; length of stay; and unplanned readmission. Oncologic outcomes included the following: R0-rate (<1 mm),[24] number of lymph nodes resected, origin, and histologic diagnosis. Only clinically relevant grade B/C complications, according to the International Study Group for Pancreatic Surgery, were included.

Ethics

Ethical approval was waived due to the observational nature of the study.

Statistical Analysis

Categorical data were reported as proportions and continuous data as mean and standard deviation or median and interquartile range (IQR) as appropriate. Data were processed and analyzed using IBM SPSS Statistics for Windows version 28.0.1 (IBM SPSS, Inc, Armonk, NY). Single imputation was used to impute missing baseline data. After imputation, PSM was performed on the complete cohort to match the robotic and the laparoscopic patients in a 1:1 ratio, using R for Mac OS X version 3.6.3. Covariates for PSM were chosen based on their potential influence on the treatment allocation and outcome. The covariates used in the PSM were the following: age higher than 70 years, sex, annual volume more than 20, BMI >30 kg/m^2, ASA 1 to 2, vascular involvement, organ involvement, previous abdominal surgery (either laparoscopic or open), comorbidity yes/no, pancreatic duct size <5 mm, tumor size, and malignant disease. Annual volume of more than 20 was not used as a covariate in the PSM in the sensitivity analysis, excluding low-volume centers. Standardized mean differences were calculated, and an standardized mean difference value of <0.01 was used to determine the optimal balance between the two groups. A caliper width between 0.1 and 0.2 was used in the PSM. After PSM, outcomes were compared pairwise using the McNemar Test in binary variables, the Wilcoxon signed rank test in continuous variables, the McNemar-Bowker test in nominal data, and the marginal homogeneity test in ordinal variables.

Sensitivity analyses were performed for the postoperative outcomes, major morbidity, operation time, blood loss, and conversion rates by excluding the learning curve effect, excluding the first 20 RPD/20 LPD and the first 30 RPD/30 LPD procedures per center, and by excluding centers with an annual RPD/LPD volume <20 based on the Miami guidelines volume criteria.[4,25-27] A new PSM was performed in these subgroups. An additional sensitivity analysis was performed using multivariable logistic regression for major morbidity and 30-day/in-hospital mortality.

Results

Overall, 2,082 patients were included, consisting of 1,006 RPD and 1,076 LPD. Of all 50 centers, 12 centers performed only RPD, 26 centers performed only LPD, and 12 centers performed both RPD and LPD. Of the 12 centers that performed both RPD and LPD, 9 centers switched from LPD to RPD during the study period.

Before Matching

Baseline Characteristics

Before PSM, the following characteristics differed significantly between RPD and LPD, respectively: ASA 1–2 (63.1% vs 77.7%; $P <$ .001), comorbidity (44.7% vs 59.6%; $P <$ .001), perioperative use of somatostatin analogs (39.8% vs 68.2%; $P <$ .001), organ involvement on preoperative computed tomography (7.5% vs 2.0%; $P <$ .001), and patients operated in a center meeting the Miami volume criteria (59.0% vs 46.7%; $P <$ .001) (Table 1).

Intraoperative Outcome

Before PSM, RPD was associated with a longer operative time (450 minutes vs 400 minutes; $P <$ .001) and a lower conversion rate (7.8% vs 18.2%, $P <$ .001), as compared with LPD (Table II).

Postoperative Outcome

Before PSM, the rates of major morbidity (33.4% vs 29.8%; $P =$ .089) and 30-day/in-hospital mortality (4.5% vs 4.7%; $P =$ .853) did not differ significantly between RPD and LPD. (Table II). For the primary outcomes, similar results were obtained after the multivariable logistic regression analysis (major morbidity (odds ratio [OR] 1.133; CI 0.932–1.376; $P =$ .209) and mortality (OR 0.902; CI 0.583–1.396; $P =$ .644). RPD was associated with a higher number of retrieved lymph nodes (17 [IQR 11–29] vs 14 [IQR 10–20], $P <$ .001), as compared with LPD. LPD was associated with lower rates of POPF grade B/C (19.4% vs 12.7%, $P <$ .001), PPH grade B/C (12.4% vs 9.3%, P = .030), DGE grade B/C (21.5% vs 7.1%, $P <$ .001), wound infection (9.0% vs 3.7%, $P <$ .001), a shorter length of stay (14 [IQR 9–24] vs 13 [IQR 9–21], $P =$ .041) (Table II). In patients with cancer (RPD $N = 617$ and LPD $N = 721$), LPD was associated with a higher R0 resection rate (70.4% vs 83.8%, $P <$ .001) as compared with RPD (Table III).

Table I
Baseline and intraoperative characteristics after RPD and LPD, before matching

Baseline	RPD $n = 1,006$	LPD $n = 1,076$	P value
Age in y, median (IQR)	67[59–74]	67 [57–73]	.179
Age >70 y, *n* (%)	382 (38.0)	389 (36.2)	.416
Sex, female, *n* (%)	480 (47.7)	529 (49.2)	.537
BMI, kg/m^2, median (IQR)	24.8 [22.6–27.6]	24.8 [22.3–27.7]	.732
BMI >30 kg/m^2, *n* (%)	125 (12.4)	140 (13.0)	.738
ASA 1–2, *n* (%)	635 (63.1)	836 (77.7)	< .001
Comorbidity, *n* (%)	450 (44.7)	641 (59.6)	< .001
Cardiac morbidity, *n* (%)	156 (15.5)	266 (24.7)	< .001
Vascular morbidity, *n* (%)	187 (18.6)	420 (39.0)	< .001
Diabetes mellitus, *n* (%)	174 (17.3)	202 (18.8)	.413
Pulmonary morbidity, *n* (%)	103 (10.2)	86 (8.0)	.088
Annual volume >20, *n* (%)	594 (59.0)	502 (46.7)	< .001
Previous abdominal surgery, *n* (%)	422 (41.9)	417 (38.8)	.150
Neoadjuvant therapy, *n* (%)	54 (5.4)	55 (5.1)	.874
Intraoperative			
Somatostatin, *n* (%)	356 (39.8)	700 (68.2)	< .001
Vascular involvement, *n* (%)	81 (8.1)	90 (8.4)	.857
Organ involvement, *n* (%)	75 (7.5)	22 (2.0)	< .001
Pancreatic duct <5 mm, *n* (%)	617 (61.3)	698 (64.9)	.104

ASA, American Society of Anesthesiologists; *BMI*, body mass index; *LPD*, laparoscopic pancreatoduodenectomy; *RPD*, robot-assisted pancreatoduodenectomy.
Bold values indicate statistical significance ($P <$ .05). Values are percentages unless mentioned otherwise.

Table II
Operative outcome after RPD and LPD, before and after matching, and in centers with an annual volume MIPD >20 with matching

Outcome	Unmatched cohort			Matched cohort			Annual volume MIPD >20		
	$n = 2,082$			$n = 1,624$			$n = 1,096$, after matching $n = 768$		
	RPD $n = 1,006$	LPD $n = 1.076$	*P* value	RPD $n = 812$	LPD $n = 812$	*P* value	RPD $n = 384$	LPD $n = 384$	*P* value
Operation time in m, median (IQR)	450 (380–533)	400 (330–490)	< .001	446 (376–530)	400 (330–487)	< .001	432 (380–501)	400 (340–490)	< .001
Blood loss in mL, median (IQR)	200 (100–400)	200 (100–400)	.235	200 (100–400)	200 (100–400)	.202	200 (100–500)	200 (100–300)	< .001
Conversion, *n* (%)	78 (7.8)	196 (18.2)	< .001	54 (6.7)	146 (18.0)	< .001	21 (5.5)	21 (5.5)	1.000
Multivisceral resection, *n* (%)	45 (4.5)	29 (2.8)	.045	27 (3.3)	25 (3.2)	.775	18 (4.7)	13 (3.5)	.584
Clavien–Dindo ≥3, *n* (%)	336 (33.4)	321 (29.8)	.089	259 (31.9)	240 (29.6)	.347	121 (31.5)	102 (26.6)	.153
Mortality 30-d /in-hospital, *n* (%)	45 (4.5)	51 (4.7)	.853	35 (4.3)	37 (4.6)	.904	13 (3.4)	18 (4.7)	.473
POPF grade B/C, *n* (%)	195 (19.4)	137 (12.7)	< .001	154 (19.0)	95 (11.7)	< .001	86 (22.4)	56 (14.6)	.006
PPH grade B/C, *n* (%)	124 (12.4)	100 (9.3)	.030	94 (11.6)	65 (8.0)	.018	41 (10.7)	32 (8.3)	.328
DGE grade B/C, *n* (%)	216 (21.5)	76 (7.1)	< .001	173 (21.4)	60 (7.4)	< .001	76 (19.8)	27 (7.0)	< .001
Bile leakage grade B/C, *n* (%)	62 (6.2)	59 (5.5)	.572	48 (5.9)	45 (5.6)	.828	35 (9.2)	20 (5.2)	.050
Postoperative drainage, *n* (%)	214 (21.3)	218 (20.3)	.605	159 (19.6)	166 (20.5)	.760	95 (24.8)	87 (22.7)	.548
Reoperation, *n* (%)	107 (13.3)	122 (11.4)	.238	85 (13.0)	85 (10.6)	.248	29 (11.0)	29 (7.7)	.560
Wound infection, *n* (%)	90 (9.0)	40 (3.7)	< .001	71 (8.8)	32 (4.0)	< .001	29 (7.6)	8 (2.1)	.001
Pneumonia, *n* (%)	70 (9.4)	28 (5.0)	.004	51 (8.9)	21 (5.0)	.223	33 (9.6)	15 (6.3)	.030
Length of stay (median [IQR])	14 (9–24)	13 (9–21)	.041	14 (9–23)	13 (9–21)	.015	13 (8–20)	11 (8–16)	.002
Readmission, *n* (%)	124 (13.2)	118 (11.6)	.318	103 (13.6)	88 (11.5)	.264	57 (15.9)	29 (8.1)	.023

Values are percentages unless mentioned otherwise.
DGE, delayed gastric emptying; *LPD,* laparoscopic pancreatoduodenectomy; *MIPD,* minimally invasive pancreatoduodenectomy; *POPF,* postoperative pancreatic fistula; *PPH,* postpancreatectomy hemorrhage; *RPD,* robot-assisted pancreatoduodenectomy.

Table III
Oncological outcome after RPD and LPD, before and after matching

Pathologic outcomes	Unmatched cohort			Matched cohort		
	RPD $n = 1,006$	LPD $n = 1,076$	*P* value	RPD $n = 812$	LPD $n = 812$	*P* value
Tumor location, *n* (%)			< .001			< .001
Pancreas	640 (82.1)	690 (66.5)		524 (82.0)	505 (65.2)	
Distal bile duct	66 (8.5)	147 (14.2)		55 (8.6)	115 (14.8)	
Ampulla of Vater	53 (6.8)	138 (13.3)		43 (6.7)	106 (13.7)	
Duodenum	17 (2.2)	58 (5.6)		15 (2.3)	46 (5.9)	
Other	4 (0.5)	5 (0.5)		2 (0.3)	3 (0.4)	
Malignant disease, *n* (%)	617 (61.3)	721 (67)	.008	507 (62.4)	522 (64.3)	.417
Histologic diagnosis, *n* (%)			< .001			.104
Adenoma	33 (3.3)	18 (1.7)		26 (3.2)	15 (1.9)	
Adenocarcinoma	617 (62.5)	720 (68.4)		507 (63.4)	521 (66.0)	
NET	58 (5.9)	74 (7.0)		51 (6.4)	63 (8.0)	
IPMN	105 (10.6)	83 (7.9)		81 (10.1)	62 (7.9)	
MCN	11 (1.1)	5 (0.5)		9 (1.1)	5 (0.6)	
Solid pseudopapillary neoplasm	8 (0.8)	25 (2.4)		7 (0.9)	23 (2.9)	
Serous cystadenoma	10 (1.0)	3 (0.3)		9 (1.1)	1 (0.1)	
Chronic pancreatitis	34 (3.4)	15 (1.4)		24 (3.0)	14 (1.8)	
Other	111 (11.2)	110 (10.4)		86 (10.8)	85 (10.8)	
Tumor size, mm, median (IQR)	25 (17–35)	25 (17–34)	.326	25 (18–35)	25 (16–34)	.114
Resection status*, R0, *n* (%)	376 (70.4)	590 (83.8)	< .001	325 (73.2)	429 (84.4)	< .001
Involved lymph nodes,* median (IQR)	2 (0–6)	1 (0–3)	< .001	2 (0–6)	1 (0–2)	< .001
Retrieved lymph nodes,* median (IQR)	17 (11–29)	14 (10–20)	< .001	16 (11–27)	14 (10–20)	.003
Adjuvant therapy,* *n* (%)	309 (56.3)	350 (59.4)	.312	266 (58.5)	254 (58.5)	.793

Values are percentages unless mentioned otherwise.
IPMN, intraductal papillary mucinous neoplasia; *IQR,* inter quartile range; *LPD,* laparoscopic pancreatoduodenectomy; *MCN,* mucinous cystic neoplasm; *NET,* neuroendovrine tumor; *RPD,* robot-assisted pancreatoduodenectomy.
* In case of malignancy.

After Matching

Baseline Characteristics

After PSM, 812 patients undergoing RPD were matched to 812 patients undergoing LPD. Hereafter, no significant differences in patient characteristics remained other than a lower use of somatostatin analogs in the RPD group and a lower number of patients operated in a center meeting the Miami volume criteria in the LPD group (Table IV). Overall, comorbidity did not differ between groups.

Table IV
Baseline and intraoperative characteristics in RPD and LPD, after matching

Baseline	RPD $n = 812$	LPD $n = 812$	P value	SMD
Age in y (median [IQR])	67 (58–74)	66 (57–73)	.312	0.058
Age >70 y, *n* (%)	304 (37.4)	297 (36.6)	.757	0.018
Sex, female, *n* (%)	396 (48.8)	384 (47.3)	.539	0.030
BMI, kg/m^2 (median [IQR])	24.7 (22.5–27.7)	24.6 (22.1–27.6)	.304	0.035
BMI >30 kg/m^2- *n* (%)	107 (13.2)	100 (12.3)	.625	0.026
ASA 1–2, *n* (%)	600 (73.9)	589 (72.5)	.503	0.031
Comorbidity, *n* (%)	404 (49.8)	415 (51.1)	.536	0.027
Cardiac morbidity- *n* (%)	128 (15.8)	188 (23.2)	< .001	0.187
Vascular morbidity- *n* (%)	178 (21.9)	288 (35.5)	< .001	0.303
Diabetes mellitus- *n* (%)	154 (19.0)	125 (15.4)	.058	0.095
Pulmonary morbidity- *n* (%)	94 (11.6)	57 (7.0)	.002	0.157
Annual volume >20, *n* (%)	436 (53.7)	396 (48.8)	.011	0.099
Previous abdominal surgery, *n* (%)	311 (38.3)	313 (38.5)	.956	0.005
Neoadjuvant therapy, *n* (%)	40 (4.9)	36 (4.4)	.716	0.023
Intraoperative				
Somatostatin, *n* (%)	282 (39.1)	521 (67.5)	< .001	0.594
Vascular involvement, *n* (%)	63 (7.8)	51 (6.3)	.271	0.058
Organ involvement, *n* (%)	17 (2.1)	21 (2.6)	.571	0.033
Pancreatic duct <5 mm, *n* (%)	508 (62.6)	517 (63.7)	.662	0.023

Values are percentages unless mentioned otherwise.
ASA, American Society of Anesthesiologists*; BMI,* body mass index; *LPD,* laparoscopic pancreatoduodenectomy; *RPD,* robot-assisted pancreatoduodenectomy; *SMD*, standard mean difference.Values are percentages unless mentioned otherwise.

Intraoperative Outcome

After PSM, RPD was associated with a longer operative time (446 min vs 400 min; $P < .001$), similar intraoperative blood loss (200 mL [IQR 100–400] vs 200 mL [IQR 100–400], $P = .202$), and a lower conversion rate (6.7% vs 18%, $P < .001$), as compared with LPD (Table II).

Postoperative Outcome

After PSM, no differences in the rates of major morbidity (31.9% vs 29.6%, $P = .347$) and 30-day/in-hospital mortality (4.3% vs 4.6%, $P = .904$) were seen between RPD and LPD, respectively. LPD was associated with lower rates of POPF grade B/C (19.0% vs 11.7%; $P < .001$), PPH grade B/C (11.6% vs 8%; $P = .018$), DGE grade B/C (21.4% vs 7.4%; $P < .001$), wound infection (8.8% vs 4.0%; $P < .001$), and shorter length of stay (14 [IQR 9–23] vs 13 [IQR 9–21]; P = .015; Table II). In patients with cancer (RPD $n = 507$ and LPD $n = 522$), LPD was associated with a higher R0 resection rate (73.2% vs 84.4%, $P < .001$). RPD was associated with a higher number of retrieved lymph nodes (16 [IQR 11–27] vs 14 [IQR 10–20], $P = .003$; Table IV).

Sensitivity Analyses

To exclude the learning curve effect, the first 20 RPD/20 LPD and the first 30 RPD/30 LPD procedures performed per center were excluded and presented in Supplementary Table S1. No significant differences were observed in major morbidity and 30-day/in-hospital mortality. The conversion rate remained significantly lower with RPD compared with LPD after excluding the first 20 RPD/LPD and first 30 RPD/LPD per center, whereas operation time, POPF grade B/C, DGE grade B/C, wound infection, and length of stay remained significantly lower with LPD.

Discussion

This first retrospective international multicenter study assessing 1,624 patients after RPD and LPD using PSM from 50 centers in 12 European countries found no significant differences in the rates of major morbidity and 30-day/in-hospital mortality. However, RPD was associated with a lower conversion rate (6.7% vs 18%) and a higher lymph node retrieval. On the other hand, LPD was associated with lower rates of POPF grade B/C, DGE grade B/C, wound infection, shorter length of stay, and a higher R0 resection rate. These differences remained consistent after excluding the first 20 and 30 RPD/LPD procedures per center. Over time, a trend toward RPD was seen in this cohort. Nine centers switched from LPD to RPD during the study period, which may suggest that these centers may have experienced some advantages or improvements with RPD compared with LPD, leading to their decision to adopt the robotic approach.

In keeping with the findings of the present study, two recent systematic reviews also found no difference in major complications between RPD and LPD.[18,19] In the present study, after PSM, the 31.9% ($n = 259$) rate of major morbidity after RPD is lower than a recent NSQIP analysis on RPD (41%, 81/193) and the multicenter Dutch LAELAPS-3 training program on RPD (44.4%, 122/275).[16,28] In contrast, two monocenter studies from expert centers reported lower rates of major morbidity, 24.8% in 500 RPDs reported from Pittsburgh and 15.7% from Beijing.[29,30] For LPD, the reported rates of major morbidity in the four published randomized trials varied from 9.4% to 50%.[12-15] This large range in the rates of major morbidity after RPD and LPD could be explained by differences in registration, surgical experience, treatment algorithms, and annual volume. The mortality after MIPD in the current study is actually expected to be somewhat higher than open pancreatoduodenectomy, given the selection of more patients with a soft pancreas and non-dilated pancreatic duct for MIPD, leading to a higher risk of postoperative pancreatic fistula.

The current study showed a longer operation time in RPD. Interestingly, a previous retrospective study from Pittsburgh demonstrated reduced operative times only after 240 RPDs meaning that with increasing experience with RPD and LPD, operative times could further decrease.[30] The higher rate of POPF grade B/C after RPD is yet unexplained. A second notable and yet unexplained outcome is the tripled rate of DGE grade B/C after RPD

(21.5% vs 7.1%; $P < .001$).[19,31] A systematic review from China reported a similar rate in DGE between RPD and LPD (OR = 0.86; 95% CI 0.68–1.10; $P = .22$).[19] However, one previous European PSM multicenter study also reported a tripled rate of DGE after RPD (20.5% vs 6.6%), as compared with LPD.[32] DGE has a multifactorial etiology, including the presence of POPF, blood loss, surgical performance, and the surgical technique used for gastric anastomosis.[22,33,34] A gastrojejunostomy reconstructed via a side-to-side anastomosis might be associated with a reduced rate of DGE grade C.[33,34] Unfortunately, no data on the type of gastro/duodenojejunostomy for RPD and LPD are available in this study.

The higher conversion rate in LPD is compatible with the four randomized trials showing conversion rates between 3% and 23.5%.[12-15] The lower conversion rate during RPD (7.8% vs 18.2%; $P < .001$) in this study is supported by a recent systematic review that included nine retrospective studies comprising 1,149 (31%) RPD and 2,583 (69%) LPD, which showed that RPD was associated with a lower conversion rate (OR = 0.45; 95% CI 0.36–0.56; $P < .001$).[19] Moreover, in a large multicenter retrospective study from the United States, RPD ($n = 409$) was also associated with lower conversion rates compared with LPD ($n = 418$) (12% vs 21%; $P < .0001$).[35] The lower need for conversion in RPD might be explained by better bleeding control, although data on the reasons for conversion are lacking.[36] Notably, the difference in the conversion rate between RPD and LPD was no longer present after excluding all centers with an annual volume <20, meaning that in high-volume centers, the LPD conversion rate is also low (Table IV).

The lower rate of R0 resections in case of malignancy after RPD in the present study is an important finding to reflect upon. This finding is not supported by the higher number of resected lymph nodes after RPD. It is difficult to reconcile both findings, given the current literature.[37] The results in the current study differ from the outcomes of recent systematic reviews from the United Kingdom and Italy, which have found no difference in R0 resection between the robotic and laparoscopic approaches.[18,38] It has been suggested that better control and better 3D vision with RPD would allow a more radical resection; however, the results of this multicenter study from high-volume leading centers in this field fail to support this expectation. It might be possible that the difference in R0 resection rate between RPD and LPD, and other observed differences, can be a greater cumulative experience with LPD during the study period. Hence, a further assessment of these differences should be performed in a few years' time. Another possibility could be that a few very high-volume centers performed the majority of LPD and RPD procedures thus impacting pathology assessment strongly. However, as LPD was performed in 38 centers and RPD in 24 centers, we do not expect such selection to have played a large role.

Study limitations

The results of this study should be interpreted in light of some limitations. First, data were collected from existing European databases, wherein differences in data collection may have introduced information bias. Because major morbidity and mortality are rather 'solid' outcomes, this is potentially less of a concern for the main study conclusions. Unmeasured confounding variables may clearly still be present. In the current study, pancreatic gland texture is missing in a considerable proportion of patients. Moreover, during the design of the registry, it was decided not to collect data on surgical technique; therefore, no data on pancreatic gland texture and technical outcomes are available in this study. Second, most of the RPD were performed in the years 2018–2020, and most of the LPD in 2014–2016 (Figure 1). Therefore, the RPD and LPD groups could be interpreted as two different time periods and might be located in different phases of the learning curve. The outcomes of the comparison between RPD and LPD would be most valid when, for both techniques the learning curve is completed. A recent systematic review reported learning curves for RPD ranging between 8 and 100 to overcome the first phase of the learning curve.[39] This could explain the relatively small impact of excluding the first 20 RPD/LPD and 30 RPD/LPD per center on the postoperative outcome (Supplementary Table S1). Third, selection bias arising from the process of patient selection for either robotic, laparoscopic, or open pancreatoduodenectomy constitutes a limitation in this study. Based on the selection criteria for minimally invasive surgery, there is, for instance, a relatively limited number of patients with vascular involvement, which may have contributed to the observed outcomes associated with the minimally invasive approaches. Unfortunately, no data regarding open pancreatoduodenectomy were included as this would clearly increase the negative impact of selection bias. Fourth, in this study, no impact was found in the sensitivity analysis for center volume/learning curve and outcomes. Notably, the data was derived from a

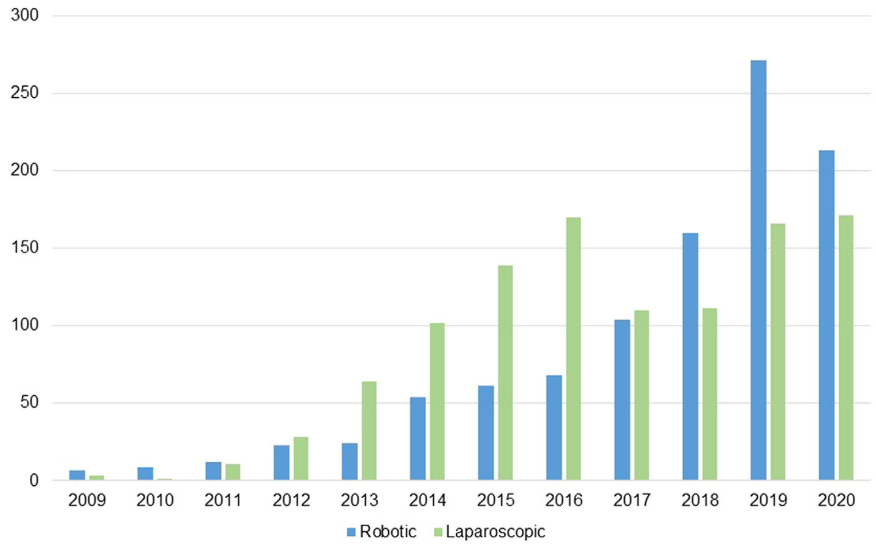

Figure. The trend in the annual use of robot-assisted pancreatoduodenectomy and laparoscopic pancreatoduodenectomy in 50 European Centers (2009–2020).

wide variety of centers with different experiences and annual volumes. Therefore, it remains challenging to quantify any association between approach and outcome. However, the results of the study give valuable insights into the outcomes of RPD versus LPD in the intermediate experience of European centers. Consequently, our results are probably generalizable to a large number of centers. Another strength of this study includes its international and multicenter design in combination with PSM. Nevertheless, PSM does not account for unknown confounders. Finally, centers were offered anonymity to reduce reporting bias.

In conclusion, this study found no difference in the rates of major morbidity and 30-day/in-hospital mortality after RPD and LPD. However, LPD showed significant benefits over RPD regarding a lower rate of POPF grade B/C, DGE grade B/C, wound infection, shorter length of stay, and a higher R0 resection rate. Operative time was marginally faster in LPD, whereas the conversion rate was substantially lower in the RPD group. RPD was associated with a higher number of retrieved lymph nodes. Future studies, preferably randomized trials, are needed to compare outcomes. Randomized trials will be hampered by the growing number of centers, which is shifting from LPD to RPD, leading to bias due to surgical experience.[16,30,40-42] The E-MIPS registry will continue to monitor outcomes after RPD and LPD in Europe.[43]

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Conflict of interest/Disclosure

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CRediT authorship contribution statement

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [https://doi.org/10.1016/j.surg.2024.02.015].

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