

Perioperative and Long-term Oncological Results of Minimally Invasive Pancreatoduodenectomy as Hybrid Technique – A Matched Pair Analysis of 120 Cases

Perioperative und onkologische Langzeitergebnisse nach minimalinvasiver Pankreatoduodenektomie in Hybridtechnik – eine Matched-Pair-Analyse von 120 Fällen



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Bibliography

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ABSTRACT

Background Laparoscopic pancreatoduodenectomy is a highly challenging procedure. The aim of this study was to analyse post-operative morbidity and mortality as well as long term overall survival in patients undergoing hybrid LPD, as

compared to open pancreaticoduodenectomy (OPD) in a single surgeon series.

Methods Patients undergoing pancreatoduodenectomy (PD) in the period from 2000 to 2015 were identified from a prospectively maintained database. All LPD procedures were performed by one specialised pancreatic surgeon (TK). Patients were matched 1 : 1 for age, sex, BMI, ASA, histological diagnosis, pancreatic texture and portal venous resection (PVR). All LPD procedures were performed as hybrid LPD – combining laparoscopic resection and open reconstruction via mini laparotomy.

Results A total of 549 patients were identified, including 489 patients in the OPD group and 60 patients in the LPD group. 60 patients were identified who underwent LPD between 2010 and 2015 versus 60 OPD patients operated in the same period. Median overall operation time was shorter in the LPD group than with OPD patients (LPD 352 vs. OPD 397 min; $p = 0.002$). Overall transfusion units were lower in the LPD group (LPD range 0–4 vs. OPD range 0–11; $p = 0.032$). Intensive care unit stay (LPD 1 vs. OPD 6 d; $p = 0.008$) and overall hospital stay (OHS: LPD 14 vs. OPD 18 d; $p = 0.012$) were shorter in the LPD groups than in the OPD group. As regards postoperative complications, LPD was associated with reduced rates of clinically relevant grade B/C postoperative pancreatic fistula (LPD 15 vs. OPD 36%; $p = 0.036$) and grade B/C delayed gastric emptying (LPD 8 vs. OPD 20%; $p = 0.049$). A total of 56 patients were diagnosed with malignant disease. The number of harvested lymph nodes and R0-resection rates were equal for LPD and OPD patients. LPD patients showed a trend to improved median overall survival (LPD mean 56 months vs. OPD mean 48 months; $p = 0.056$).

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Conclusion Hybrid LPD is a safe procedure associated with a reduction in clinically relevant postoperative complications and allows faster recovery. Long term oncological outcome of hybrid LPD for malignant disease is equal to that with the standard open approach.

ZUSAMMENFASSUNG

Hintergrund Ziel dieser Studie war es, die postoperative Morbidität und Mortalität sowie Langzeit-Gesamtüberlebensraten bei Patienten nach laparoskopischer Pankreatoduodenektomie (LPD) in Hybridtechnik im Vergleich zur offenen Pankreatoduodenektomie (OPD) anhand der Serie eines LPD-spezialisierten Pankreaschirurgen zu analysieren.

Material und Methoden Daten von Patienten, die im Zeitraum 2000–2015 eine Pankreatoduodenektomie (PD) erhalten haben, wurden einer prospektiv geführten Datenbank entnommen. Alle LPD-Resektionen wurden von einem Chirurgen (TK) durchgeführt. Es erfolgte ein 1 : 1 Matching der Patienten anhand der Parameter Alter, Geschlecht, BMI, ASA, Histologie, Textur des Pankreasparenchyms und Durchführung einer Pfortaderresektion. Alle LPD-Resektionen wurden in Hybridtechnik mit laparoskopischer Resektion und anschließender Rekonstruktion mittels Minilaparotomie durchgeführt.

Ergebnisse Insgesamt konnten 549 Patienten anhand der Datenbank identifiziert werden, 489 Patienten in der OPD-

Gruppe und 60 Patienten in der LPD-Gruppe. 60 LPD-Patienten aus dem Zeitraum 2010–2015 und 60 OPD-Patienten aus dem Zeitraum 2000–2015 wurden in die Studie eingeschlossen. Die mediane Operationszeit in der LPD-Gruppe war verkürzt im Vergleich zur OPD-Gruppe (LPD 352 vs. OPD 397 min; $p = 0,002$). Die Anzahl perioperativ benötigter Erythrozytenkonzentrate war geringer in der LPD-Gruppe (LPD 0–4 vs. OPD 0–11; $p = 0,032$). Die mediane Dauer der intensivmedizinischen Therapie (LPD 1 vs. OPD 6 d; $p = 0,008$) und die mediane Gesamtdauer des Krankenhausaufenthalts (LPD 14 vs. OPD 18 d; $p = 0,012$) waren kürzer in der LPD-Gruppe im Vergleich zur offenen Resektion. Die LPD war mit einer geringeren Rate klinisch relevanter Grad-B/C-Pankreasfisteln (LPD 15 vs. OPD 36%; $p = 0,036$) und verzögerter Magenentleerung Grad B/C assoziiert (LPD 8 vs. OPD 20%; $p = 0,049$). 56 der eingeschlossenen Patienten wiesen eine maligne Raumforderung auf. Die Anzahl resezierter Lymphknoten und die Rate an R0-Resektionen waren vergleichbar in der LPD- und der OPD-Gruppe. Bei LPD-Patienten zeigte sich der Trend einer verbesserten medianen Gesamtüberlebensrate (LPD 56 vs. OPD 48 Monate; $p = 0,056$).

Schlussfolgerung Die LPD in Hybridtechnik ist eine sichere Technik, die mit der Reduktion klinisch relevanter postoperativer Komplikationen assoziiert ist und eine schnelle postoperative Erholung erlaubt. Die onkologischen Langzeitergebnisse nach LPD in Hybridtechnik bei malignen Befunden sind gleichwertig zur offenen Technik.

Introduction

Minimal invasive techniques are emerging in abdominal surgery. As a rationale, laparoscopic approaches are associated with reduced postoperative morbidity, faster recovery, and a shorter overall hospital stay [1, 2]. The role of minimally invasive resections in pancreatic surgery remains an issue of debate [3, 4]. Laparoscopic pancreatoduodenectomy (LPD) is a sophisticated procedure performed by a few mainly high-volume centers worldwide. A recent analysis of the National Cancer Database (NCDB), including 4421 pancreatoduodenectomy (PD) patients, demonstrated that only 9% of patients were undergoing LPD [5].

The first LPD procedure was reported in 1994 by Gagner and Pomp [6]. In the past years, several alternative minimally invasive PD techniques were described. Currently, the most frequently applied techniques include the totally laparoscopic PD (TLPD), the robot-assisted approach (RAPD), and the hybrid resection, combining laparoscopic resection consecutively followed by a mini-laparotomy for specimen extraction and open reconstruction [7, 8]. Recent meta-analyses demonstrate the beneficial effects of LPD procedures regarding short-term postoperative outcome. De Rooij et al. and Correa-Gallego et al. found a prolonged operation time, reduced blood loss, and a shorter overall hospital stay in patients undergoing LPD compared to open pancreatoduodenectomy (OPD) [8, 9]. No randomized controlled trials comparing LPD and OPD are available to date.

Most studies evaluating LPD include patients with small, mainly benign, lesions [9]. Consequently, only a few studies regarding oncologic safety and long-term outcome of LPD are available. Recent single-center analyses found equivalent long-term overall survival rates in patients undergoing LPD compared to OPD [10, 11].

RAPD procedures and TLPD are well-characterized by several retrospective and registry studies, whereas data regarding hybrid PD remain rare and the studies currently available present conflicting results [12–14]. The aim of this study was to assess postoperative morbidity and mortality as well as long-term overall survival in patients undergoing hybrid LPD compared to standard OPD.

Methods

Patients undergoing PD in the period from 2000 to 2015 were identified from a prospectively maintained database. The retrospective analysis was approved by the ethics review committee of the University of Luebeck following the German guideline of ethics approval by the German National Medical Association. The data of 80 patients included in this analysis were already published in a recent study evaluating the early results and technical aspects of hybrid LPD [14]. For the current study, the patient cohort was enlarged by 40 patients, and we present long-term oncologic results. A histopathological workup was performed according to a standardized protocol, and was retrospectively con-

firming by a pathologist blinded to all clinical and histological data. Baseline parameters included age, sex, body mass index (BMI), and American Society of Anesthesiologists (ASA) score. The pathologic tumor stage was defined according to the AJCC (American Joint Committee on Cancer). Overall operation time and overall transfusion units were reevaluated in all patients. Short-term outcome parameters included overall hospital stay (OHS), intensive care unit stay (ICU), and postoperative morbidity. Complications were recorded following the Clavien-Dindo classification (CDC) system. Pancreatic fistulae (POPF), delayed gastric emptying (DGE), and postpancreatectomy hemorrhage (PPH) were defined according to the International Study Group of Pancreatic Surgery (ISGPS) definitions [15–17]. Propensity score matching was performed, and patients were matched 1:1 for age, sex, BMI, ASA, histological diagnosis, pancreatic texture, and portal venous resection (PVR) using SPSS software. An LPD was performed using the hybrid technique involving laparoscopic resection and open reconstruction via minilaparotomy, as previously described [14]. This is a single-surgeon laparoscopic series, and all laparoscopic operations were performed by one specialized pancreatic surgeon (TK) at the departments of surgery of the University of Luebeck (2012–2015) and the University of Freiburg (2010–2012). Open PD was performed by three specialized pancreatic surgeons at the department of surgery of the University of Freiburg, while standards of PD remained constant. Perioperative management and treatment of postoperative complications were standardized. Statistical analysis was executed with SPSS Software 21.0® (IBM SPSS Statistics, IBM Corporation, Chicago, IL). The chi-squared test and t-test as well as Mann-Whitney U and Kruskal-Wallis test were used when appropriate for statistical testing at a significance level of $p = 0.05$. Survival analysis was done using the stepwise Cox proportional hazard model. Univariate analysis and log-rank test were performed, and all parameters with p -values < 0.1 were included in the multivariate analysis.

Results

A total number of 549 patients were identified from our single-center prospectively maintained database, including 489 OPD and 60 LPD patients. After propensity score matching, 60 LPD versus 60 OPD patients were analyzed. Follow-up in the OPD and LPD groups was performed from 2000 until 2015 and 2010 until 2015, respectively. Patient demographics and baseline parameters were well balanced (► **Table 1**). There was a total of 31 (26%) patients with periampullary adenocarcinoma (PAMPAC), 25 (21%) patients with pancreatic adenocarcinoma (PDAC), and 21 (18%) were diagnosed with a cystic neoplasm of the pancreas (CNP), including intraductal papillary mucinous neoplasm (IPMN), serous cystic neoplasm (SCN), and mucinous cystic neoplasm (MCN). Another 13 (11%) patients had chronic pancreatitis and 11 (9%) had a neuroendocrine tumor (NET). The percentage of R0 resections were similar in LPD and OPD groups (LPD 89% vs. OPD 82%; $p = 0.414$). The median overall operation time was shorter in the LPD group compared to the OPD patients (LPD 352 min vs. OPD 397 min; $p = 0.002$). Overall transfusion units were reduced in the LPD group (LPD range 0–4 vs. OPD range 0–11; $p = 0.032$). ICU (LPD 1 day vs. OPD 6 days; $p = 0.008$) and OHS

► **Table 1** Baseline parameters: TNM classification and margin status for all malignant diseases and neuroendocrine tumors.

	LPD (n = 60)	OPD (n = 60)	P value
Age (y; median, range)	65.5 (20–83)	63 (29–82)	0.528
Sex (m:f)	24:36	26:34	0.715
BMI (median, range)	24.5 (15.5–39)	24 (16–33)	0.693
ASA (%)			1.000
▪ I	8 (13)	8 (13)	
▪ II	36 (60)	36 (60)	
▪ III	16 (27)	16 (27)	
Pancreatic texture (%)			0.841
▪ hard	17 (28)	16 (27)	
▪ soft	43 (72)	44 (73)	
Histology n (%)			0.550
▪ ductal adenocarcinoma	12 (20)	13 (22)	
▪ periampullary cancer	14 (23)	17 (28)	
▪ cystic neoplasia	16 (27)	5 (8)	
▪ chronic pancreatitis	4 (7)	9 (15)	
▪ neuroendocrine tumor	5 (8)	6 (10)	
▪ other	9 (15)	10 (17)	
pT (n)			
▪ T1	7 (21)	3 (8)	0.431
▪ T2	5 (15)	10 (26)	
▪ T3	19 (57)	22 (56)	
▪ T4	2 (7)	4 (10)	
pN (n)			
▪ N+	15 (45)	21 (54)	0.485
▪ N0	18 (55)	18 (46)	
Margin status (n)			
▪ R+	4 (11)	8 (18)	0.414
▪ R0	31 (89)	36 (82)	

LPD: laparoscopic pancreatoduodenectomy; OPD: open pancreatoduodenectomy; BMI: body mass index; ASA score: American Society of Anesthesiologists score.

(LPD 14 days vs. OPD 18 days; $p = 0.012$) were shorter in the LPD group compared to the OPD group. Regarding postoperative complications, LPD was associated with reduced rates of clinically relevant grade B/C POPF (LPD 15% vs. OPD 36%; $p = 0.036$) and grade B/C DGE (LPD 8% vs. OPD 20%; $p = 0.049$). The 30-day (LPD 0% vs. OPD 3%; $p = 0.496$) and 90-day mortality (LPD 2% vs.

► **Table 2** Perioperative results.

	LPD	OPD	P value
OR time (min; median, range)	352 (212–510)	397 (262–625)	0.002
Transfusion (units; median, range)	0 (0–4)	0 (0–11)	0.032
Reoperation rates	22%	20%	0.83
30-Day mortality	0%	3%	0.496
In-hospital mortality	2%	3%	1.000
90-Day mortality	2%	3%	1.000
ICU (days; median, range)	1 (0–22)	6 (1–78)	0.008
OHS (days; median, range)	14 (1–59)	18 (9–149)	0.012
SSI	13%	22%	0.217
Pneumonia	10%	12%	0.798
CDC n (%)			0.436
▪ 0–2	44 (73)	42 (71)	
▪ 3/4	16 (27)	16 (26)	
▪ 5	–	2 (3)	
DGE n (%)			0.049
▪ A/none	55 (92)	42 (70)	
▪ B/C	5 (8)	12 (20)	
▪ N/A	0 (0)	6 (10)	
POPF n (%)			0.036
▪ A/none	51 (85)	38 (64)	
▪ B/C	9 (15)	22 (36)	
PPH n (%)			0.908
▪ A/None	55 (92)	52 (87)	
▪ B/C	5 (8)	8 (13)	

OR time: overall operation time; ICU: intensive care unit; CDC: Clavien-Dindo classification; DGE: delayed gastric emptying; POPF: postoperative pancreatic fistula; PPH: postpancreatectomy hemorrhage; SSI: surgical site infection; OHS: overall hospital stay.

OPD 3%; $p = 1.000$) were comparable in both groups. Reoperation rates as well as surgical site infections, PPH, and pneumonia rates were not different in both groups (► **Table 2**). The most frequent indication for reoperation in both groups was PPH at the pancreatic anastomosis (for details ► **Table 3**).

A total of 56 patients were diagnosed with malignant tumors (PDAC and PAMPAC), 26 in the LPD group and 30 in the OPD group. PAMPAC and PDAC patients most commonly had T3 tumors (49 and 84%, respectively). For PDAC, the median number of lymph nodes resected was not different in the LPD and OPD groups (LPD 17 vs. OPD 15; $p = 0.461$), as well as for PAMPAC (LPD 13 vs. OPD 16; $p = 0.131$) (► **Table 4**). Two patients were initially diagnosed with benign disease, and less than 10 lymph nodes were resected. In the final histopathological diagnosis, the lesions were classified as partly malignant. The number of resected lymph nodes was at least 10 in all other patients. Sixty-seven percent of LPD PDAC patients and 69% of OPD patients re-

► **Table 3** Indications for reoperations.

	LPD	OPD
Reoperations total n (%)	13 (100)	12 (100)
Pancreatic texture		
▪ soft	10 (77)	11 (92)
▪ hard	3 (23)	1 (8)
PPH pancreatic anastomosis	3 (23)	4 (33)
PPH other site	2 (15)	2 (17)
POPF	1 (8)	1 (8)
Intra-abdominal abscess	3 (23)	1 (8)
SSI	1 (8)	1 (8)
Bile leak	1 (8)	0
Lymphatic fistula	0	1 (8)
Other indications	2 (15)	2 (17)

PPH: postpancreatectomy hemorrhage; POPF: postoperative pancreatic fistula; SSI: surgical site infection. Other indications: second look after intraoperative bleeding, thrombosis of major vessels, pancreatic necrosis.

ceived adjuvant chemotherapy with gemcitabine. For details of the adjuvant chemotherapy in PDAC and PAMPAC patients, ► **Table 5**. Concerning survival analysis, three LPD patients were lost to follow-up and could not be included in the analysis. PVR, sex, and R-status qualified as prognostic factors in univariate analysis ($p = 0.001$, $p = 0.047$, $p = 0.032$ respectively). Multivariate analysis disclosed the following independent prognostic factors: Portal vein resection [HR 8.3 (SE 0.7); $p = 0.005$], surgical access [HR 5.8 (SE 0.7); $p = 0.012$], and sex [HR 0.3 (SE 0.7); $p = 0.043$] (► **Table 6**). For malignant disease, patients undergoing LPD showed a trend of improved median overall survival (LPD 56 months vs. OPD 48 months; $p = 0.056$) (► **Fig. 1**).

Discussion

Minimal invasive techniques are being increasingly established in pancreatic surgery [1, 3, 8]. For distal pancreatectomy, laparoscopic approaches are widely in use and are gaining acceptance as an equivalent alternative procedure to standard open resections [18–20]. LPD remains an issue of debate as the procedure is technically demanding, and is associated with a flat learning curve, even in experienced pancreatic surgeons [14, 21]. Only a few surgeons worldwide routinely perform LPD, and a main part of studies evaluating the safety and outcome of LPD are single surgeon series [8, 10].

A growing number of studies directly comparing OPD and LPD demonstrate LPD as a feasible and safe procedure [9, 22, 23]. Mainly in terms of perioperative blood loss, the OHS and postoperative complication rates in LPD are superior to OPD [8, 9, 12, 24]. Most trials available to date evaluate TLPD or RAPD, but data comparing hybrid LPD and OPD remain rare. Only two recent meta-analyses assessing LPD versus OPD also include a small percentage of hybrid LPDs [8, 12], and only a few large hybrid LPD series have been published so far [14, 23].

► **Table 4** Malignant histology.

	LPD		OPD		P value
	n	%/range	n	%/range	
PDAC	12		13		
pT					0.326
▪ T1	2	17	1	8	
▪ T2	0	0	0	0	
▪ T3	10	83	11	84	
▪ T4	0	0	1	8	
pN					0.543
▪ N+	8	67	7	54	
▪ N0	4	33	6	66	
LN total	17	0–25	15	5–25	0.461
PAMPAC	14		17		
pT					0.88
▪ T1	1	7	0	0	
▪ T2	4	29	7	41	
▪ T3	7	50	8	47	
▪ T4	2	14	2	12	
pN					0.186
▪ N+	4	33	9	53	
▪ N0	10	67	8	47	
LN total	13	2–33	16	10–32	0.131

PDAC: pancreatic ductal adenocarcinoma; PAMPAC: periampullary adenocarcinoma; LN total: number of lymph nodes harvested in total.

To the best of our knowledge, we present the largest matched-pair analysis comparing hybrid LPD versus OPD, assessing postoperative morbidity and mortality as well as long-term overall survival and oncologic outcome. Our study is the first to demonstrate a shorter overall operation time for LPD compared to OPD. As a potential cause, the vast majority of analyses studied TLPD and RAPD involving laparoscopic reconstruction [8, 9, 24]. Hybrid LPD may offer a faster reconstruction via minilaparotomy (5–8 cm), especially in an experienced high-volume center of pancreatic surgery. As another factor explaining shorter operation times in the LPD group, the indication for reoperation was liberally made in these patients in the presence of tumor adhesion to the mesenterico-portal vein. The rationale was to assure patient safety by not prolonging the operation time due to technical difficulties. There was no difference in the T stage comparing LPD and OPD patients, and 1:1 matching was performed for histological diagnosis and BMI, so a bias of these parameters regarding operation time is unlikely.

Our study disclosed reduced perioperative blood loss and less clinically relevant postoperative complications such as POPF and DGE for hybrid LPD in analogy to other studies evaluating minimally invasive PD techniques, herein showing the benefits of minimally invasive resections [10, 22, 25, 26]. A recent systematic literature review compared TLPD, RAPD, and hybrid LPD showing in-

► **Table 5** Adjuvant chemotherapy for malignant disease.

	LPD	OPD
PDAC n (%)	12 (100)	13 (100)
▪ adjuvant gemcitabine	8 (67)	9 (69)
▪ adjuvant other	0	3 (23)
▪ no adjuvant therapy	3 (25)	2 (15)
PAMPAC	14 (100)	17 (100)
▪ adjuvant gemcitabine	3 (21)	1 (6)
▪ adjuvant other	1 (7)	1 (6)
▪ no adjuvant therapy	10 (72)	15 (88)

PDAC: pancreatic ductal adenocarcinoma; PAMPAC: periampullary adenocarcinoma.

creased blood loss and higher rates of POPF in hybrid LPD patients compared to the other LPD techniques [13]. However, only 16% of the patients included in the analysis received hybrid LPD. These patients were derived from a very small series and the techniques of hybrid LPD are heterogeneous.

In accordance with larger LPD series and a recent meta-analysis, our study disclosed a reduction of clinically relevant DGE in LPD patients [8, 10, 27]. The functional cause, however, remains an issue of debate. As a potential mechanism, a prospective study by Marjanovic et al. found a reduction of postoperative bowel edema in patients undergoing LPD compared to OPD, reducing postoperative impaired bowel movement and peristaltic [28].

Our study found no difference in reoperation rates for LPD and OPD patients in contrast to a recent meta-analysis [24]. A large LPD series showed varying reoperation rates of up to 29% [9, 14, 23]. While reoperation rates in series of PD for PDAC remain as low as 10% or less [29, 30], reoperation rates in our study were 22% for LPD and 20% for OPD patients. A high percentage of patients selected for LPD presented with benign disease (57%) and soft pancreatic texture (LPD group 72% vs. OPD 73%), resulting in an increased risk of postoperative morbidity [31]. The most frequent cause of reoperation in our study was intragastric bleeding at the pancreatic anastomosis (pancreatogastrostomy), which was regularly managed by reexploration at our institution.

Our study demonstrated no difference in lymph node yield, R0 resection rates and long-term overall survival in patients undergoing LPD versus OPD for malignant disease. Only two large LPD series assessed long-term overall survival rates in patients presenting with PDAC or periampullary cancers showing equivalent 5-year overall survival rates [10, 11]. Most likely as a result of pooling PDAC and periampullary cancer associated with better prognosis, overall survival rates were prolonged compared to overall survival rates reported for PDAC patients after curative resection [30]. In terms of radical oncologic resection rates, two recent meta-analyses found a higher number of lymph nodes harvested and reduced R1 resection rates in patients undergoing LPD [8, 12]. As a potential cause, patients selected for LPD mainly presented with small tumors, on average 10 mm in size, that did not infiltrate large vessels or other organs [12]. In our study, a high

► **Table 6** Overall survival. Variables with P-values <0.10 in univariate analysis were included into multivariate analysis. P-values were derived from the two-sided log rank test (univariate) and the Cox proportional hazards regression model (multivariate).

Parameter	n	Deaths [n]	Median [month]	SE mean	univariate		multivariate		
				HR	p (univ)	SE HR	p (multiv)		
Access	LPD	21	4	5					
	OPD	30	12	48	9	5,8	0,056	0,7	0,012
Histo	PDAC	22	9	36	5				
	PAMPAC	29	7	69	10	2,5	0,082	0,6	0,141
PVR	PVR +	7	4	19	7				
	PVR 0	44	12	65	8	8,3	0,001	0,7	0,005
Sex	m	20	3	68	7				
	w	31	13	51	10	0,3	0,047	0,7	0,043
R-Status	R+	7	4	25	7	e		e	e
	R0	43	12	64	8	e	0,032	e	e
N	N+	24	10	50	11	e		e	e
	N0	27	6	61	7	e	0,062	e	e

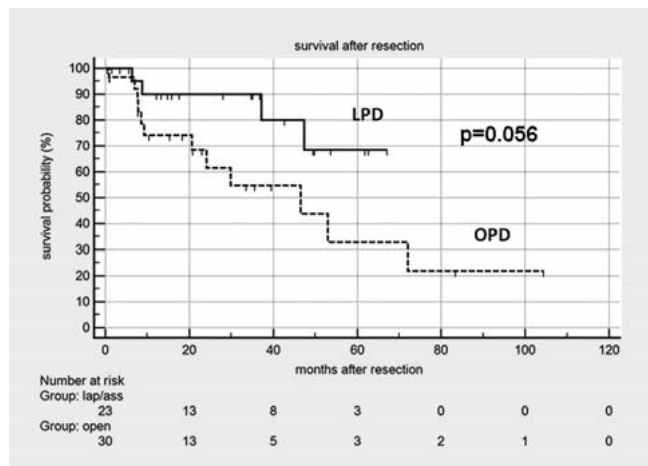
PVR: portal vein resection; SE: standard error; HR: hazard ratio; univ: univariate, multiv: multivariate, e: excluded from stepwise multivariate cox regression

rate of patients diagnosed with T3 tumors (50%) were undergoing LPD. Consequently, radical oncologic resection can also be performed safely by LPD in patients presenting with an advanced T stage.

We found a trend of improved overall survival in patients receiving LPD compared to OPD. An earlier onset of adjuvant chemotherapy and less treatment delay in LPD patients due to reduced clinically relevant postoperative complications and a shorter OHS may be a relevant effect, but could not be evaluated in this study. Croome et al. similarly demonstrated a higher rate of LPD patients receiving early adjuvant chemotherapy compared to OPD patients [10]. The authors even found a benefit in terms of progression-free survival for the LPD group. As a high rate of both LPD and OPD patients received adjuvant gemcitabine or other agents, differing rates of adjuvant chemotherapy in both groups were not a determinant of improved overall survival in the LPD group.

Conclusion

In summary, we present the largest series directly comparing hybrid LPD versus OPD. Hybrid LPD is associated with factors that are commonly encountered in laparoscopic resections as a reduction of perioperative blood loss and overall operation time, as well as clinically relevant POPF and DGE, allowing for faster recovery and a shorter OHS. The long-term oncologic outcome of hybrid LPD for malignant disease is equal to the standard open approach. As a limitation, the study was performed retrospectively. However, in the absence of randomized controlled trials on the subject of LPD, a matched-pair analysis directly comparing LPD to OPD is the most valid approach for comparison. In the future, randomized controlled trials are warranted to determine safety and long-term outcomes of LPD in both techniques – totally laparoscopic and with hybrid.



► **Fig. 1** Overall survival in patients with malignant disease. LPD: laparoscopic pancreatoduodenectomy; OPD: open pancreatoduodenectomy, p-value derived from the log-rank test.

Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Bausch D, Keck T. Laparoscopic pancreatic resections. *Langenbecks Arch Surg* 2013; 398: 939–945
- [2] Guillou PJ, Quirke P, Thorpe H et al. Short-term endpoints of conventional versus laparoscopic-assisted surgery in patients with colorectal cancer (MRC CLASICC trial): multicentre, randomised controlled trial. *Lancet* 2005; 365: 1718–1726

- [3] Postlewait LM, Kooby DA. Laparoscopic distal pancreatectomy for adenocarcinoma: safe and reasonable? *J Gastrointest Oncol* 2015; 6: 406
- [4] Nakamura M, Nakashima H. Laparoscopic distal pancreatectomy and pancreatoduodenectomy: is it worthwhile? A meta-analysis of laparoscopic pancreatectomy. *J Hepatobiliary Pancreat Sci* 2013; 20: 421–428
- [5] 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
- [6] Gagner M, Pomp A. Laparoscopic pylorus-preserving pancreatoduodenectomy. *Surg Endosc* 1994; 8: 408–410
- [7] Zureikat AH, Moser AJ, Boone BA et al. 250 robotic pancreatic resections: safety and feasibility. *Ann Surg* 2013; 258: 554–562
- [8] de Rooij T, Lu MZ, Steen MW et al. Minimally invasive versus open pancreatoduodenectomy: systematic review and meta-analysis of comparative cohort and registry studies. *Ann Surg* 2016; 264: 257–267
- [9] Correa-Gallego C, Dinkelspiel HE, Sulimanoff I et al. Minimally-invasive vs. open pancreaticoduodenectomy: systematic review and meta-analysis. *J Am Coll Surg* 2014; 218: 129–139
- [10] Croome KP, Farnell MB, Que FG et al. Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches? *Ann Surg* 2014; 260: 633–640
- [11] Stauffer JA, Coppola A, Villacreses D et al. Laparoscopic versus open pancreatoduodenectomy for pancreatic adenocarcinoma: long-term results at a single institution. *Surg Endosc* 2017; 31: 2233–2241
- [12] Nigri G, Petrucciani N, La Torre M et al. Duodenopancreatectomy: open or minimally invasive approach? *Surgeon* 2014; 12: 227–234
- [13] Boggi U, Amorese G, Vistoli F et al. Laparoscopic pancreaticoduodenectomy: a systematic literature review. *Surg Endosc* 2015; 29: 9–23
- [14] Wellner UF, Küsters S, Sick O et al. Hybrid laparoscopic versus open pylorus-preserving pancreatoduodenectomy: retrospective matched case comparison in 80 patients. *Langenbecks Arch Surg* 2014; 399: 849–856
- [15] Bassi C, Dervenis C, Butturini G et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. *Surgery* 2005; 138: 8–13
- [16] 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
- [17] Grützmann R, Rückert F, Hippe-Davies N et al. Evaluation of the International Study Group of Pancreatic Surgery definition of post-pancreatectomy hemorrhage in a high-volume center. *Surgery* 2012; 151: 612–620
- [18] Venkat R, Edil BH, Schulick RD et al. Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity compared to the open technique: a systematic review and meta-analysis. *Ann Surg* 2012; 255: 1048–1059
- [19] Pericleous S, Middleton N, McKay SC et al. Systematic review and meta-analysis of case-matched studies comparing open and laparoscopic distal pancreatectomy: is it a safe procedure? *Pancreas* 2012; 41: 993–1000
- [20] Sharpe SM, Talamonti MS, Wang E et al. The laparoscopic approach to distal pancreatectomy for ductal adenocarcinoma results in shorter lengths of stay without compromising oncologic outcomes. *Am J Surg* 2015; 209: 557–563
- [21] Speicher PJ, Nussbaum DP, White RR et al. Defining the learning curve for team-based laparoscopic pancreaticoduodenectomy. *Ann Surg Oncol* 2014; 21: 4014–4019
- [22] Asbun HJ, Stauffer JA. Laparoscopic vs. open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. *J Am Coll Surg* 2012; 215: 810–819
- [23] Dokmak S, Ftériche FS, Aussilhou B et al. The largest European single-center experience: 300 laparoscopic pancreatic resections. *J Am Coll Surg* 2017; 225: 226–234.e2
- [24] Zhang J, Wu WM, You L et al. Robotic versus open pancreatectomy: a systematic review and meta-analysis. *Ann Surg Oncol* 2013; 20: 1774–1780
- [25] 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
- [26] Lai EC, Yang GP, Tang CN. Robot-assisted laparoscopic pancreaticoduodenectomy versus open pancreaticoduodenectomy – a comparative study. *Int J Surg* 2012; 10: 475–479
- [27] Tee MC, Croome KP, Shubert CR et al. Laparoscopic pancreatoduodenectomy does not completely mitigate increased perioperative risks in elderly patients. *HPB (Oxford)* 2015; 17: 909–918
- [28] 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
- [29] Crippa S, Cirocchi R, Randolph J et al. Pancreaticojejunostomy is comparable to pancreaticogastrostomy after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. *Langenbecks Arch Surg* 2016; 401: 427–437
- [30] Lillemoe KD, Yeo CJ, Cameron JL. Pancreatic cancer: state-of-the-art care. *CA Cancer J Clin* 2000; 50: 241–268
- [31] Hu BY, Wan T, Zhang WZ et al. Risk factors for postoperative pancreatic fistula: Analysis of 539 successive cases of pancreaticoduodenectomy. *World J Gastroenterol* 2016; 22: 7797