



# Minimally Invasive Pancreatoduodenectomy: Contemporary Practice, Evidence, and Knowledge Gaps

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## ABSTRACT

Minimally invasive pancreatoduodenectomy has gained popularity throughout the last decade. For laparoscopic pancreatoduodenectomy, some high-level evidence exists, but with conflicting results. There are currently no published randomized controlled trials comparing robotic and open pancreatoduodenectomy. Comparative long-term data for patients with pancreatic ductal adenocarcinoma is lacking to date. Based on the existing evidence, current observed benefits of minimally invasive pancreatoduodenectomy over open pancreatoduodenectomy seem scarce, but retrospective data indicate the

safety of these procedures in selected patients. As familiarity with the robotic platform increases, studies have shown an expansion in indications, also including patients with vascular involvement and even indicating favorable results in patients with obesity and high-risk morphometric features. Several ongoing randomized controlled trials aim to investigate potential differences in short- and long-term outcomes between minimally invasive and open pancreatoduodenectomy. Their results are much awaited.

**Keywords:** Adenocarcinoma; Laparoscopic; Minimally invasive surgery; Pancreatoduodenectomy

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### Key Summary Points

Minimally invasive pancreatoduodenectomy has gained popularity throughout the last decade.

For laparoscopic pancreatoduodenectomy, some high-level evidence exists with conflicting results.

Familiarity with the robotic platform shows an expansion in indications and there has been an increased awareness of structured training and patient selection for minimally invasive pancreatoduodenectomy.

Comparative long-term data for patients with pancreatic ductal adenocarcinoma are lacking to date, but several ongoing randomized controlled trials exist.

## INTRODUCTION

In the past three decades, great advancements in minimally invasive techniques (laparoscopic and robotic-assisted) have been made in the field of gastrointestinal surgery, including cancer surgery. Minimally invasive surgery (MIS) now accounts for approximately 69–80% of all colorectal cancer surgery according to some reports [1, 2]. In Norway, the laparoscopy rate for colon and rectal cancer is 85% [3]. For these procedures, laparoscopy has proven itself to be equal [4, 5] or even superior [6, 7] to the traditional open approach with regards to short- and long-term outcomes. Also, the use of MIS for the treatment of upper gastrointestinal cancer has increased [8], and following the publication of randomized controlled trials and systematic reviews, rates are steadily growing for liver surgery [9–12] and laparoscopic distal pancreatectomy [13, 14]. With advantages such as less blood loss, faster recovery, and shortened length-of-stay (LOS) compared with open surgery, there has been a transition into making

MIS the standard treatment modality for several malignant diseases in the gastrointestinal tract [15]. However, a similar adoption to MIS for the pancreatoduodenectomy (PD) has been slow.

The PD is a complex abdominal surgical procedure with a considerable morbidity and mortality profile. Even though the first laparoscopic pancreatoduodenectomy (LPD) was reported in 1994 [16], routine use of minimally invasive techniques for PD has only gained popularity in selected centers [17]. Some reasons for this are the complexity of the procedure, cost of the equipment and the time and volume needed for training. Also, results from randomized controlled trials (RCT) and other comparative studies have failed to show a clear benefit [18]. Even though the first robotic pancreatoduodenectomy (RPD) was performed in 2001 [19], larger reports on this procedure have not emerged until recently [20]. For both LPD and RPD, high-level evidence data are both conflicting and limited when compared to traditional open surgery.

This invited opinion article aims to address the contemporary practice and current level of evidence concerning minimally invasive pancreatoduodenectomy (MIPD). In addition, we aim to identify potential knowledge gaps in the existing literature concerning differences in MIPD versus open PD. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## METHODS

A narrative review was conducted in PubMed/MEDLINE using the search terms alone and in combination of “minimally invasive” AND “pancreatoduodenectomy” OR “robotic pancreatoduodenectomy” OR “laparoscopic pancreatoduodenectomy”. The search period ended as of January 31, 2022. Studies published prior to 2011 were excluded. Reference lists of all included papers and related articles were screened manually to identify potential missed but relevant studies. Moreover, a search was conducted at the World Health Organization

(WHO) trial registry database (trialssearch.who.int/) in order to identify ongoing trials investigating MIPD using the same search terms. The final inclusion of papers and ongoing trials to cite and reference was made at the discretion of the authors.

## CURRENT EVIDENCE

### Laparoscopic Pancreatoduodenectomy

#### *Single-Center Studies*

Throughout the past decade, numerous retrospective studies have compared laparoscopic versus open PDs (Table 1). The majority of these publications have been single-center case-control studies or propensity scored-matched studies. The studies that define how patients were selected for either open or laparoscopic surgery show a tendency to select patients with smaller tumors and no sign of vascular invasion for laparoscopy [21–28]. Vascular infiltration requiring major vascular resection and reconstruction alone, however, is not a contraindication to MIPD and can be safely performed with identical graft patency compared to OPD when performed by expert surgeons, as shown in the study by Crome et al. [29].

Several studies find no difference in perioperative or oncological outcomes. However, the study by Asbun et al. compared 53 laparoscopic pancreatoduodenectomies (LPD) to 215 open pancreatoduodenectomies (OPD) and found a higher lymph node yield in the LPD-group (23 vs. 17,  $p = 0.007$ ) [30]. In addition, several studies found that LPD is associated with a longer operative time and some show less blood loss and shorter LOS with LPD. Dokmak et al. found higher rates of grade C pancreatic fistula (24 vs. 6%,  $p = 0.007$ ), bleeding (24 vs. 7%,  $p = 0.02$ ) and reoperations (24 vs. 11%,  $p = 0.09$ ) in the LPD group. In the subgroup analysis of patients with ductal adenocarcinoma, these observed differences were not statistically significant [24].

In the single-center study by Croome et al., comparing 108 patients operated by LPD to 214 patients operated by OPD, LPD also resulted in shorter hospital stay (6 vs. 9 days,  $p < 0.001$ ),

significant longer progression-free survival ( $p = 0.03$ ) and shorter time to functional recovery, resulting in faster initiation of adjuvant chemotherapy [23].

#### *Multicenter Studies*

Several nationwide and multicenter studies have been published or are still ongoing [32–36]. Sharpe et al. found a higher 30-day mortality rate in patients treated laparoscopically (OR 1.89,  $p = 0.009$ ), using data from the National Cancer Database. This difference was not significant when centers that had performed less than ten procedures during the study period of 2 years were excluded [32]. Data from a nationwide Japanese database identified that patients treated laparoscopically were younger and had less comorbidities compared to OPD, with a higher overall complication rate in the latter group (41 vs. 26%,  $p = 0.005$ ). However, using propensity score matching, there were no differences in outcome between LPD and OPD [35].

#### *Randomized Controlled Trials*

Since 2017, four RCTs have been published comparing LPD with OPD (Table 2). The first two trials were single-center trials finding shorter hospital stay in the LPD group [37] as well as lower rate of major complications [38]. None of these trials found any differences in oncological outcomes. The LEOPARD-2 study from the Netherlands was terminated before reaching the planned inclusion size because of safety concerns in the interim analysis, as the 90-day mortality rate was higher in the LPD group (10 vs. 4%;  $p = 0.20$ ) [39]. The recent multicenter randomized controlled study by Wang et al. found a significantly shorter LOS in the LPD group (median 15.0 vs. 16.0 days,  $p = 0.02$ ), with no differences in 90-day mortality or serious postoperative morbidities [40]. The findings from the first three RCTs have been evaluated in a recently published meta-analysis. LDP was not associated with any advantages over OPD. A high risk of bias and moderate-to-very-low certainty of evidence was found [41].

**Table 1** Published studies investigating potential differences in laparoscopic versus open pancreatoduodenectomy (significant differences between LPD and OPD are indicated by bold characters)

Study, year	Country	Patients, <i>n</i> (LPD vs. OPD)	Indication	Operative time, min (LPD vs. OPD)	Blood loss, ml (LPD vs. OPD)	LOS, days (LPD vs. OPD)	Major morbidity, % (LPD vs. OPD)	30-day mortality, % (LPD vs. OPD)	Long-term outcome (for PDAC)
Zureikat et al. (2011) [21]	USA	14 vs. 14 <sup>a</sup>	All indications for PD. Smaller tumors in laparoscopy group	<b>456 vs. 372</b>	300 vs. 400	8 vs. 8.5	20 vs. 7	7 vs. 0%	NA
Asbun et al. (2012) [30]	USA	53 vs. 215	All indications for PD, without need for major portal vein resection in laparoscopy group	<b>541 vs. 401</b>	<b>195 vs. 1032</b>	<b>8 vs. 12</b>	24 vs. 24	5 vs. 8%	NA
Mesleh et al. (2013) [22]	USA	75 vs. 48	All indications for PD, without need for segmental vein resection	<b>551 vs. 355</b>	NA	7 vs. 8	31 vs. 31	NA	NA
Croome et al. (2014) [23]	USA	108 vs. 214	PDAC	379 vs. 387	<b>492 vs. 866</b>	<b>6 vs. 9</b>	5 vs. 13	1 vs. 2%	Same OS, but longer PFS for LPD
Dokmak et al. (2015) [24]	France	46 vs. 46 <sup>a</sup>	Selected patients with small periampullary lesions	<b>342 vs. 264</b>	368 vs. 293	25 vs. 23	28 vs. 20	2 vs. 0	NA
Song et al. (2015) [25]	South Korea	93 vs. 93 <sup>a</sup>	Selected patients with benign and low-grade malignant tumors	<b>480 vs. 347</b>	609 vs. 570	<b>14 vs. 19</b>	7 vs. 5	0 vs. 0	ND in 5-year survival

**Table 1** continued

Study, year	Country	Patients, <i>n</i> (LPD vs. OPD)	Indication	Operative time, min (LPD vs. OPD)	Blood loss, ml (LPD vs. OPD)	LOS, days (LPD vs. OPD)	Major morbidity, % (LPD vs. OPD)	30-day mortality, % (LPD vs. OPD)	Long-term outcome (for PDAC)
Tan et al. (2015) [26]	China	30 vs. 30	All indications	513 vs. 371	NA	9 vs. 11	0.1 vs. 0.1	0 vs. 0	NA
Stauffer et al. (2017) [31]	USA	58 vs. 193	PDAC	518 vs. 375	250 vs. 600	6 vs. 9	22 vs. 30	3 vs. 5	ND in OS
Zhou et al. (2019) [27]	China	55 vs. 93 <sup>a</sup>	PDAC	330 vs. 260	150 vs. 200	13 vs. 14	10 vs. 14	0 vs. 2	ND in OS
Shin et al. (2019) [28]	South Korea	56 vs. 56 <sup>a</sup>	Periampullary tumors in elderly patients ( $\geq 70$ years)	321 vs. 268	468 vs. 362	13 vs. 15	5 vs. 10	NA	ND in OS or DFS

*LOS* length of stay, *PDAC* pancreatic ductal adenocarcinoma, *NA* not available, *ND* no difference, *OS* overall survival, *PFS* progression-free survival, *DSF* disease-free survival

<sup>a</sup>Propensity-matched groups

**Table 2** Published randomized controlled studies on laparoscopic versus open PD

Name of study and author	Year	Country	Study design	Number of patients included	Inclusion criteria	Outcomes
PLOT Palanivelu et al. [37]	2017	India	Single-center, non-blinded RCT	32 LPD vs. 32 OPD	All malignancies requiring a PD Patients aged 30–70 years	Shorter hospital stays for LPD More blood loss and higher surgical site infection for OPD
PADULAP Poves et al. [38]	2018	Spain	Single-center, non-blinded RCT	34 LPD vs. 32 OPD	All conditions (benign or malignant) requiring a PD Patients aged 18 years or older	Reduced major morbidity and shorter LOS for LPD No differences in oncological outcomes
LEOPARD-2 van Hilst et al. [39]	2019	The Netherlands	Multicenter, patient-blinded RCT	50 LPD vs. 49 OPD	All conditions (benign and malignant) requiring a PD Patients aged 18 years or older	Higher mortality rate for LPD
Wang et al. [40]	2021	China	Multicenter, non-blinded RCT	297 LPD vs. 297 OPD	All conditions (benign and malignant) requiring a PD Patients aged 18–75 years	Shorter hospital stay for LPD Longer operative time, less blood loss and fewer blood transfusions for LPD Mobilization, oral food intake, and removal of nasogastric tube all happened 1 day earlier for LPD

### Robotic Pancreatoduodenectomy

Overall, the results from retrospective studies on RPD reflect those seen for LPD, as RPD is associated with an increase in operative time and less blood loss when compared with OPD (Table 3) [42–49]. Chen et al. stratified patients by year of surgery and discovered that the difference in operative time was not significant by the last year of inclusion [50]. Yan et al. conducted a meta-analysis of 13 studies that included 2403 patients, 33% of which underwent a robotic procedure. Compared to open

surgery, they found shorter LOS and no differences in overall complication or mortality rates [20].

A recently published large registry study based on data from the National Cancer Database found similar long-term survival for RPD and OPD when performed for PDAC, with a median survival of 22.0 and 21.8 months, respectively [55]. For certain subgroups of patients, RPD have shown superior outcomes compared to OPD. Varley et al. found evidence that RPD was associated with improved outcomes for patients with high-risk morphometric

**Table 3** Published studies investigating potential differences in robotic versus open pancreatoduodenectomy (significant differences between RPD and OPD are indicated by bold characters)

Study, year	Country	Patients, (RPD vs. OPD)	Indication	Operative time, min (RPD vs. OPD)	Blood loss, ml (RPD vs. OPD)	LOS, days (RPD vs. OPD)	Major morbidity, % (RPD vs. OPD)	30-day mortality, % (RPD vs. OPD)	Long-term outcome for PDAC
Buchs et al. (2011) [48]	USA	44 vs. 39	Pancreatic tumors without vascular invasion	444 vs. 559	387 vs. 827	13 vs. 14	NA	4.5 vs. 2.6	NA
Zhou et al. (2011) [44]	China	8 vs. 8	Not specified	718 vs. 420	153 vs. 210	16 vs. 24	NA	NA	NA
Baker et al. (2016) [51]	USA	22 vs. 49	All patients requiring a PD	454 vs. 364	425 vs. 650	7 vs. 9	13 vs. 20	0 vs. 4.1	NA
Zureikat et al. (2016) [49]	USA	211 vs. 817	Pancreatic tumors without vascular invasion	402 vs. 300	200 vs. 300	8 vs. 8	23 vs. 23	1.9 vs. 2.8	NA
Boggi et al. (2016) [52]	Italy	83 vs. 36	Selected patients requiring a PD (not locally advanced, BMI < 35)	527 vs. 425	NA	17 vs. 14	16 vs. 6	1.2 vs. 0	ND in OS or DFS
McMillan et al. (2017) [43]	USA	152 vs. 152 <sup>a</sup>	Pancreatic tumors without major vascular invasion	NA	No difference	6 vs. 10	23 vs. 23	3.3 vs. 1.3	NA
Napoli et al. (2018) [53]	Italy	82 vs. 227 <sup>a</sup>	Selected patients requiring PD (i.e., no vascular invasion)	502 vs. 450	452 vs. 782	18 vs. 18	7 vs. 10	NA	NA
Kauffmann et al. (2019) [42]	Italy	20 vs. 24 <sup>a</sup>	Primary resectable PDAC (no vascular invasion) in patients with a BMI < 35	548 vs. 480	851 vs. 982	17 vs. 15	12 vs. 3	NA	ND in OS or DFS
Weng et al. (2021) [45]	China	105 vs. 210 <sup>a</sup>	Primary resectable PDAC (no vascular invasion)	300 vs. 300	300 vs. 300	17 vs. 17	13 vs. 15	0 vs. 1.0	ND in OS or DSF
Mulchandani et al. (2021) [54]	India	21 vs. 27	Not clearly defined	440 vs. 414	259 vs. 404	11 vs. 14	NA	3.7 vs. 4.8	NA

Table 3 continued

Study, year	Country	Patients, (RPD vs. OPD)	Indication	Operative time, min (RPD vs. OPD)	Blood loss, ml (RPD vs. OPD)	LOS, days (RPD vs. OPD)	Major morbidity, % (RPD vs. OPD)	30-day mortality, % (RPD vs. OPD)	Long-term outcome for PDAC
Bencini et al. (2020) [46]	Italy	35 vs. 35 <sup>a</sup>	Pancreatic tumors without vascular invasion	530 vs. 335	NA	8 vs. 10	17 vs. 17	2.9 vs. 0	NA
Shyr et al. (2022) [47]	Taiwan	65 vs. 65 <sup>a</sup>	All patients with PDAC requiring a PD	510 vs. 462	251 vs. 562	NA	6 vs. 6	0 vs. 0	ND in OS

LOS length of stay, PDAC pancreatic ductal adenocarcinoma, OS overall survival, DFS disease-free survival, ND no difference

<sup>a</sup>Propensity-matched groups

features [56], and in a retrospective series from Pittsburgh and UCLA, the robotic approach was analyzed comparing obese to non-obese patients, using a BMI > 30 for obesity. In obese patients, use of robotic approach was associated with a decrease in wound infection, bleeding, and clinically relevant postpancreatectomy fistula, while preserving other perioperative outcomes compared to the open approach. As obesity increases all postoperative complications, the authors speculate if robotic surgery may offset some of these in the obese population [57].

### Knowledge Gaps and Ongoing Trials

Based on the studies included in this audit, there are still unanswered questions, particularly concerning long-term oncological outcomes, quality of life (QoL), and more advanced resections in patients with vascular invasion. According to the World Health Organization (WHO) trial registry database (trialsearch.who.int/), there are currently 11 ongoing RCTs that compare the different modalities, one of which is comparing LPD with RPD (Table 4). Only three of these studies are designed with the primary focus on oncological outcomes. As with previous RCTs, LOS remains the primary endpoint in several of the ongoing studies.

## DISCUSSION

PD remains a challenging procedure, despite improved preoperative strategies and advances made in peri- and postoperative care. It is still associated with a high morbidity and mortality rate compared to other elective procedures for malignant disease. As such, every effort should be made to improve these outcomes. A relevant question is whether a transition to MIS can achieve this. So far, the data from the existing published literature have failed to demonstrate any clear and reproducible, clinically relevant improvement despite the inherent selection bias towards favorable features for MIS within the studies.



This review identified four completed RCTs investigating potential differences in LPD vs. OPD, finding conflicting results regarding short-term outcomes. As previously mentioned, data on long-term outcomes from published retrospective trials are limited or even lacking. Hence, current endpoints and gains from open or MIPD must be discussed based on short-term outcomes and potential benefits to the immediate recovery after surgery. Importantly, no RCTs have been published so far showing potential benefits of LPD over OPD concerning long-term outcomes. For RPD, several retrospective and propensity-score matched studies have also failed to identify any major improvement in LOS, major morbidities, or postoperative mortality when compared to OPD. Furthermore, no completed RCT has yet been published investigating potential differences in outcomes for RPD versus OPD. Four trials are registered as either recruiting or pending at the WHO trial registry.

The initial published RCTs on LPD vs. OPD (PLOT and PADULAP) found that LPD was associated with a shorter hospitalization time than OPD. Both of these studies are limited by small sample sizes ( $N = 64$  and  $66$  patients, respectively).

The PLOT-trial by Palanivelu et al. [37] included a relatively young and healthy population. The mean age was 58 and 57 years in the open and laparoscopic group, respectively. Approximately half of the patients in each group had no comorbidities and the comorbidities listed in the other half ranged from diabetes to heart disease.

In the PADULAP-trial by Poves et al. [38], they found a 4-day difference in LOS (median 13.5 vs. 17 days;  $p = 0.024$ ) and a lower rate of severe complications after LPD (15.6 vs. 37.9%,  $p = 0.048$ ). However, nine out of the 32 patients in the laparoscopy group that had a resectable disease were converted to open surgery, primarily due to intraoperative findings of vascular involvement or uncontrolled bleeding. Importantly, besides highly selected patients included, both the PLOT and PADULAP studies were single-center, single-surgeon RCTs, thus limiting the external validity of the results.

The LEOPARD-2 study [39] was first designed as a phase 2 study, assessing safety of the laparoscopic modality. As the safety proved to be acceptable, more patients were included in a phase 3 study. Despite no difference in severe complications (Clavien Dindo  $\geq$  III), they observed a trend towards a higher mortality rate in the laparoscopy group. Ninety-nine out of the 105 patients that initially were randomized to either laparoscopic or open procedure underwent surgery. Five out of 50 in the laparoscopy group died within 90 days after surgery compared to two out of 49 in the open group. This difference was not significant (risk ratio [RR] 4.90 [95% CI 0.59–40.44];  $p = 0.20$ ), but still resulted in a premature termination of the study. The deaths in the laparoscopy group were due to vascular damage (superior mesenteric vein and/or superior mesenteric artery) in two patients, post pancreatectomy hemorrhage in two patients and grade C pancreatic fistula in one patient. There was a conversion rate of 20% in the laparoscopy group, and the reason for conversions were either vascular involvement, bleeding, or severe inflammation. The authors concluded that the safety concerns were unexpected, as the procedures were performed in the setting of trained surgeons performing more than 20 or more PDs annually and that experience, learning curves, and volume might have influenced outcomes. Nevertheless, despite the unexpected results from this trial, safe implementation to avoid a negative impact of the learning curve on clinical outcomes is of great importance for both LPD and RPD [58, 59]. Interestingly, a recent systematic review found no significant difference in the learning curve for RPD versus LPD, even though the findings were limited by the retrospective nature and heterogeneity of the published studies [60].

The most recent and largest published RCT to date by Wang et al. [40] managed to overcome the concern with experience and learning curve. The surgeons involved in this study were well experienced, and each surgeon had performed more than 100 LPDs. The primary improvement of LPD versus OPD was a 1-day reduction (15 vs. 16 days) in LOS. As addressed in an accompanying editorial, the extensive

**Table 4** Planned and ongoing trials comparing MIPD with OPD

Primary study name	Country	Year initiated	Recruitment status	Indication	Arms	Primary outcome	Design	N
NCT02807701	Egypt	2016	Completed	Small tumors without vascular invasion	LPD vs. OPD	LOS	RCT	40
NCT03138213	China	2017	Recruiting	Malignant disease requiring a PD	LPD vs. OPD	LOS	RCT	656
NCT03172572	Netherlands	2017	Completed	All patients requiring a PD	MIPD (not specified LPD or RPD) vs. OPD	Major morbidity	Triple-blinded Multicenter	4220
NCT03722732	India	2018	Recruiting	Periapillary carcinoma	LPD vs. OPD	Bleeding	RCT	36
NCT03747588	China	2018	Not yet recruiting	Malignant disease requiring a PD and no more than 180 degrees affection of the SMV	LPD vs. OPD	Bleeding, intraabdominal infection, overall complications, POPF	RCT	100
NCT03785743	China	2018	Not yet recruiting	Malignant disease requiring a PD	LPD vs. OPD	5-year OS, DFS	RCT	200
ChiCTR1900024490	China	2019	Pending	All patients requiring a PD	RPD vs. LPD	POPF, morbidity	RCT	100
NCT03870698	South Korea	2019	Recruiting	Periapillary tumors without vascular invasion	LPD vs. OPD	Functional recovery	RCT	252
				BMI < 30				

**Table 4** continued

Primary study name	Country	Year initiated	Recruitment status	Indication	Arms	Primary outcome	Design	N
NCT04171440	USA	2019	Recruiting	All patients requiring a PD without vascular invasion	MIS-PD (LPD and RPD) vs. OPD	Time to functional recovery	RCT Patient-blinded	240
NCT04400357	China	2020	Recruiting	All patients (BMI < 35) requiring a PD without vascular invasion	RPD vs. OPD	Time to functional recovery, percentage of patients with adenocarcinoma who reach adjuvant treatment	RCT Patient-blinded	244
ChiCTR2000038932	China	2020	Recruiting	All patients requiring a PD	RPD vs. OPD	LOS	Multicenter RCT	100
DRKS00022026	Germany	2020	Pending	Primary resectable and borderline resectable pancreatic cancer without neoadjuvant treatment	MIS-PD (LPD and RPD) vs. OPD	Perioperative tumor cell dissemination	Non-randomized controlled trial	90
DRKS00020407	Germany	2020	Recruiting	All patients requiring a PD without vascular invasion	RPD vs. OPD	Overall morbidity	RCT Open label	80

learning curve may not relate to the marginal benefit [61].

Importantly, most of the RCTs have focused on LOS and functional recovery as the benchmarks of improvement. However, LOS as a primary endpoint must be interpreted with caution, as this is likely highly affected by local logistical issues or social and cultural factors. Lastly, high-level evidence on the oncological outcomes of minimally invasive distal pancreatectomy is underway [62], and findings from this study might be extrapolated to MIPD.

In regards to patient selection, all the RCTs except from the study by Wang et al. excluded patients with vascular involvement. In the PADULAP and the PLOT trials, as well as the study by Wang et al., patients who received neoadjuvant chemotherapy were also excluded. The LEOPARD trial excluded patients who received neoadjuvant radiotherapy. Given the current trend towards neoadjuvant treatment, even in patients with primary resectable ductal adenocarcinomas [63], one could argue that this excludes a group of patients that is expected to increase in the future. There is also an increase in the use of PD for patients with borderline and locally advanced pancreatic cancer, often requiring vascular resection and reconstruction. It remains to be shown what role MIS has for these patients. Both neoadjuvant radiochemotherapy and the addition of biliary stents, which are often required in this setting, creates more inflammation and potentially a more challenging operative field. However, a recent review investigating patient selection, volume criteria, and training programs for RPD concluded that RPD is safe and feasible for all indications when performed by specifically trained surgeons working in centers who can maintain a minimum volume of 20 RPDs annually [64]. Also, a Dutch multicenter training program in RPD revealed that an expansion in initial inclusion criteria was possible based on individual surgical experience resulting in venous resection being performed in 6% of the cases [58]. With structured training programs and increasing familiarity with the robotic platform, there is reason to believe that more reports on advanced resections will emerge in the future.

## CONCLUSIONS

The compelling advantages of minimally invasive techniques, such as for colorectal cancer, are yet to be clearly documented for PD. The current observed benefits of LPD over OPD seem scarce, based on existing evidence. There has been an increased awareness in structured training and patient selection for MIPD. As familiarity with the robotic platform increases, studies have shown an expansion in indications. Whether or not this transforms into clinically relevant benefits for the patients remains unanswered. Results from ongoing trials investigating potential differences in MIPD and OPD are much awaited, and will hopefully shed more light to the potential gain with the minimal invasive platform for PD.

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