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
MINIMALLY INVASIVE PANCREATODUODENECTOMY — A REVIEW OF THE LITERATURE AND CURRENT PRACTICE

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 (trialsearch.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 pancreateoduodenectomies (LPD) to 215 open pancreateoduodenectomies (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, n (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 | 456 vs. 372 | 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 | 541 vs. 401 | 195 vs. 1032 | 8 vs. 12 | 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 | 551 vs. 355 | NA | 7 vs. 8 | 31 vs. 31 | NA | NA |
| Croome et al. (2014) [23] | USA | 108 vs. 214 | PDAC | 379 vs. 387 | 492 vs. 866 | 6 vs. 9 | 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 | 342 vs. 264 | 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 | 480 vs. 347 | 609 vs. 570 | 14 vs. 19 | 7 vs. 5 | 0 vs. 0 | ND in 5-year survival |
| Study, year | Country | Patients, n (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\(^a\) | 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\(^a\) | Periampullary tumors in elderly patients (> 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, *DFS* disease-free survival

\(^a\)Propensity-matched groups
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 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 |
| 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. 152a            | 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. 227a             | 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. 24a              | 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. 210a            | 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                          |
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, postpancreatectomy 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
| 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                                     | Multicenter  | 4220|
| NCT03722732        | India     | 2018           | Recruiting         | Periampullary 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         | Periampullary tumors without vascular invasion | LPD vs. OPD                   | Functional recovery                                   | RCT          | 252|
| 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 Patient-blinded | 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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