Minimally Invasive Versus Open Distal Pancreatectomy (LEOPARD)

A Multicenter Patient-blinded Randomized Controlled Trial

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Objective: This trial followed a structured nationwide training program in minimally invasive distal pancreatectomy (MIDP), according to the IDEAL framework for surgical innovation, and aimed to compare time to functional recovery after minimally invasive and open distal pancreatectomy (ODP).

Background: MIDP is increasingly used and may enhance postoperative recovery as compared with ODP, but randomized studies are lacking.

Methods: A multicenter patient-blinded randomized controlled superiority trial was performed in 14 centers between April 2015 and March 2017. Adult patients with left-sided pancreatic tumors confined to the pancreas without vascular involvement were randomly assigned (1:1) to undergo MIDP or ODP. Patients were blinded for type of surgery using a large abdominal dressing. The primary endpoint was time to functional recovery. Analysis was by intention to treat. This trial was registered with the Netherlands Trial Register (NTR5689).

Results: Time to functional recovery was 4 days [interquartile range (IQR) 3–6) in 51 patients after MIDP versus 6 days (IQR 5–8) in 57 patients after ODP ($P < 0.001$). The conversion rate of MIDP was 8%. Operative blood loss was less after MIDP (150 vs 400 mL; $P < 0.001$), whereas operative time was longer (217 vs 179 minutes; $P = 0.005$). The Clavien–Dindo grade ≥III complication rate was 25% versus 38% ($P = 0.21$). Delayed gastric emptying grade B/C was seen less often after MIDP (6% vs 20%; $P = 0.04$). Postoperative pancreatic fistulas grade B/C were seen in 39% after MIDP versus 23% after ODP ($P = 0.07$), without difference in percutaneous catheter drainage (22% vs 20%; $P = 0.77$). Quality of life (day 3–30) was better after MIDP as compared with ODP, and overall costs were non-significantly less after MIDP. No 90-day mortality was seen after MIDP versus 2% (n = 1) after ODP.

Conclusions: In patients with left-sided pancreatic tumors confined to the pancreas, MIDP reduces time to functional recovery compared with ODP. Although the overall rate of complications was not reduced, MIDP was associated with less delayed gastric emptying and better quality of life without increasing costs.

Keywords: distal pancreatectomy, IDEAL, laparoscopic, minimally invasive, pancreatic surgery, robot-assisted

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Pancreatic resections are complex surgical procedures with a strong volume–outcome relationship.[1] Distal pancreatectomy is performed for symptomatic benign, premalignant, and malignant disease of the pancreatic body or tail.[2] Although distal pancreatectomy is associated with less morbidity than pancreatoduodenectomy, it remains a major abdominal operation associated with a 30% to 50% risk of complications and 1% to 4% risk of death.[2–6]

Distal pancreatectomy has traditionally been performed using an open approach, but in the past decade, the minimally invasive approach using laparoscopic surgery or robot-assisted surgery has become increasingly popular.[7,8] Pooled data of observational studies, generally from single, high-volume expert centers, have suggested that minimally invasive distal pancreatectomy (MIDP) is associated

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with shorter length of hospital stay, compared with open distal pancreatectomy (ODP).[9,10] Despite this potential benefit, MIDP is only used in about one-third of patients according to a recent analysis of the National Surgical Quality Improvement Program (NSQIP) database.[11] This may be related to the complex nature of minimally invasive pancreatic surgery and the lack of randomized studies describing the benefits for this approach in time to functional recovery, quality of life, and costs.[4,7,10,12]

In the past, the uncontrolled introduction of minimally invasive surgical techniques (eg, cholecystectomy, colorectal surgery) initially led to an increase in complication rates.[13,14] Following these results, multiple appeals were made over the past 20 years to standardize the development and implementation of new surgical procedures.[15] We aimed to safely introduce MIDP according to the IDEAL framework for surgical innovation through a nationwide training program.[16–18] Following this program, the use of MIDP in the Netherlands increased seven-fold, with outcomes comparable to those from expert centers.[19,20] As the next step according to IDEAL, a nationwide, multicenter, patient-blinded, randomized controlled trial was designed to determine whether MIDP improves time to functional recovery compared with ODP.

METHODS

Design and Patients

The design and rationale of the LEOPARD trial has been published previously.[21] This investigator-initiated, multicenter, patient-blinded, randomized controlled superiority trial was performed in 14 centers of the Dutch Pancreatic Cancer Group, and followed the CONSORT guideline.[22] All patients provided written informed consent before randomization. This trial complies with the Declaration of Helsinki. The institutional review boards of all participating centers approved the study protocol. The authors were responsible for the design and analysis of the study, and take full responsibility for the integrity and completeness of the data, the contents of this article, and the fidelity of this article to the trial protocol. Adults with an indication for elective distal pancreatectomy because of symptomatic benign, premalignant, or malignant left-sided pancreatic tumors were eligible for randomization. The Yonsei criteria[23] were followed, meaning that tumors had to be confined to the pancreas with an intact posterior pancreatic fascial layer, and at least 1 cm distant from the celiac artery. Excluded were patients with a tumor larger than 8 cm, who required resection of organs other than pancreas or spleen, who had undergone radiotherapy for pancreatic cancer, who had chronic pancreatitis (according to the M-ANNHEIM criteria), who were pregnant, or who participated in another study with potential interference of the primary study endpoint.

Randomization and Blinding

Patients were blinded with a large abdominal dressing until all criteria of functional recovery were met.[21] Efficacy of blinding was assessed at day 3 and at the time that functional recovery was met by asking patients which surgical procedure they believed to have undergone. Blinding of the entire team of surgeons and nurses was considered not possible in this nationwide trial. All patients were treated within an enhanced recovery setting including early mobilization and oral intake on demand. Patients were randomly assigned in a 1:1 ratio to undergo either MIDP or ODP, using an online randomization module (ALEA, Clinical Research Unit, Amsterdam UMC, Amsterdam, the Netherlands). Permuted-block randomization was used with concealed block sizes of 2 to 6 to ensure equal group numbers. Randomization was stratified by center volume (<10 vs ≥ 10 distal pancreatectomies per year) and type (university vs non-university teaching hospital), and indication for surgery (malignant vs nonmalignant tumor).

Surgical Quality Control

Quality criteria were determined before patients were enrolled in the study. MIDP was performed by surgeons who completed the dedicated LAELAPS training program for MIDP in the Netherlands,[20] had performed >50 advanced minimally invasive gastrointestinal procedures (ie, beyond diagnostic laparoscopy, cholecystectomy, and appendectomy), >20 distal pancreatectomies (either MIDP or ODP), and >5 MIDPs. As a quality control measure, every first MIDP per center was recorded on video and anonymously scored by an expert (MAH) using the method described by Birkmeyer et al.[24] The minimum score was set at 3 out of 5 for every domain (ie, gentleness, tissue exposure, instrument handling, time and motion, and flow of the operation). All participating centers performed at least 20 pancreatoduodenectomies annually according to the nationwide Dutch volume threshold for pancreatic surgery. In the Netherlands, there is no specific volume threshold for distal pancreatectomy.

Procedures

Technical details of MIDP and ODP, as performed within the trial, were published previously.[21] Steps were essentially similar for MIDP and ODP, but some variation (eg, trocar placement, stump closure, drain placement) at the discretion of the operating surgeon was allowed.

Outcomes

The primary endpoint was time to functional recovery (days) after surgery, defined as all of the following: independently mobile at the preoperative level, sufficient pain control with oral medication alone, ability to maintain at least 50% daily required caloric intake, no intravenous fluid administration, and no clinical signs of infection when other criteria were met. When patients deteriorated after meeting all criteria for functional recovery, the last moment of functional recovery was recorded. Time to functional recovery is regarded as a more objective outcome measure than hospital stay as the latter is frequently influenced by external factors. Individual components of the primary endpoint were analyzed as secondary endpoint. Secondary endpoints also included complications, feeding tube placement, percutaneous catheter drainage, surgical reinterventions, length of hospital stay, intensive care unit admission, readmission, quality of life (ie, EQ-5D-3L questionnaire at 1, 3, 5, 14, 30, 90 days postoperatively, and QLQ-C30 questionnaire at 14, 30, 90 days postoperatively), and costs (additional information is shown in the supplemental digital content, http://links.lww.com/SLA/B496). Follow-up was up to 90 days postoperatively. Data collection was performed by local physicians using printed case record forms, and cross-checked with primary sources by the study coordinators (TR, JH). Clinical outcomes were evaluated by three investigators in pancreatic surgery (ie, adjudication committee) independently, who were all blinded for treatment allocation. Definitions used in this trial are shown in the supplemental digital content (http://links.lww.com/SLA/B496). Discrepancies were resolved on the basis of consensus by the adjudication committee.

Sample Size Calculation and Statistical Analyses

Based on a nonparametric test, we calculated that 108 patients were needed to detect a 2-day reduction in postoperative time to functional recovery, with a power of 80% $(1-\beta)$ and a 2-sided α level of 0.05. The 2-day reduction was based on observational data.[19,20,25] Patients who did not undergo surgery for reasons unrelated to the surgical procedure were replaced according to protocol.

All analyses were performed according to the intention-to-treat principle. Differences in dichotomous outcomes were assessed using the chi-square test or Fisher exact test, as appropriate. Differences in continuous outcomes were assessed using the independent-samples *t* test or the Mann–Whitney *U* test, as appropriate. The primary endpoint was analyzed likewise, ignoring censoring of observations, because all patients were expected to reach the primary endpoint within 90 days after distal pancreatectomy. Dichotomous outcomes were presented as relative risks (RRs) with corresponding 2-sided 95% confidence intervals (CIs). Continuous outcomes were either presented as means with standard deviations (SDs), or as medians with interquartile ranges (IQRs), depending on the data distribution. Potential interactions between stratification parameters (center volume, center type, and indication for surgery) and the primary endpoint were assessed in a multivariable Cox regression analysis. Missing quality-of-life data were imputed according to predictive mean matching principles, using 10 imputations. No imputation was performed for patients in whom all quality-of-life data were missing. A linear mixed model was used to analyze differences in quality-of-life scores over time, adjusted for baseline values. Details on cost analysis are shown in the supplemental digital content (http://links.lww.com/SLA/B496). Healthcare costs from the hospital's perspective were compared using nonparametric bootstrapping, drawing 1000 samples of the same sizes as the original samples and with replacement. Costs were presented as mean differences with corresponding 2-sided 95% bias corrected and accelerated confidence intervals (BCaCIs). A 2-sided *P* value of less than 0.05 was considered statistically significant. Adjustment for multiple testing was not performed. Per protocol and as treated analyses are shown in the supplemental digital content (http://links.lww.com/SLA/B496).

Role of the Funding Source

The LEOPARD trial was an investigator-initiated trial supported by an unrestricted grant from Johnson & Johnson Medical Limited (Livingston, UK), which was used to cover salary costs of the trial coordinators. The funders had no role in the study design, data collection, data analysis, data interpretation, writing the manuscript or the submission process.

RESULTS

Between April 9, 2015 and March 15, 2017, a total of 181 patients with left-sided symptomatic benign, premalignant, or malignant pancreatic tumors were screened for eligibility. A total of 111 patients from 14 centers were randomized (Fig. 1), of whom 3 patients did not undergo surgery because of reasons unrelated to the surgical approach (1 emigrated, 1 withdrew consent to undergo surgery, and 1 for poor medical condition) and were replaced according to the study protocol. Baseline characteristics were comparable for both groups (Table 1).

Overall, 51 patients were assigned to MIDP, of whom 47 underwent MIDP (42 laparoscopic, and 5 robot-assisted), 2 patients did not undergo resection due to intraoperatively diagnosed metastatic disease, 1 patient underwent ODP because of tumor progression, and 1 patient only required laparoscopic adrenalectomy. In all centers, the first MIDP procedure met the quality requirements as defined in the protocol.[21] Four MIDPs (8%) were converted to ODP, because of adhesions (n = 2) and lack of adequate exposure through the minimally invasive approach (n = 2). Blinding was maintained up to functional recovery in 39 patients (76%), of whom 13 patients (25%) believed to have undergone ODP, 10 patients (20%) correctly believed to have undergone MIDP, 3 patients (6%) were unclear, and for 13 (25%) patients, it was unknown which procedure they believed to have undergone.

Overall, 57 patients were assigned to ODP, of whom 55 underwent ODP, 1 patient had intraoperatively detected metastases and underwent a palliative gastrojejunostomy bypass, and 1 patient underwent open pancreatic enucleation. Blinding was maintained in 41 patients (72%), of whom 21 patients (37%) believed to have undergone MIDP, 10 patients (18%) correctly believed to have undergone ODP, 3 patients (5%) were unclear, and for 7 patients (12%), it was unknown which procedure they believed to have undergone.

All patients reached functional recovery within 90 days postoperatively. Functional recovery was reached after a median of 4 days (IQR 3–6) for MIDP and 6 days (IQR 5–8) for ODP ($P < 0.001$). Moreover, every criterion of functional recovery was reached more rapidly after minimally invasive than ODP (Table 2).

Operative time was longer after MIDP [217 (IQR 135–277) vs 179 (129–231) minutes; $P = 0.005$], whereas blood loss was less [150 (50–350) vs 400 (200–775) mL; $P < 0.001$]. The pancreas was transected using a stapler device in 92% versus 88% of patients ($P = 0.45$). Oncological outcomes in patients diagnosed with pancreatic ductal adenocarcinoma [microscopically radical resection margins 7/13 vs 4/10 patients; $P = 0.51$; and total number of resected lymph nodes 11 (IQR 5–19) vs 15 (IQR 5–22) nodes; $P = 0.71$] did not differ between MIDP and ODP. Operative and pathology outcomes are shown in Table 3.

Postoperative complications are shown in Table 4. Length of initial hospital stay was 2 days shorter after MIDP [median 6 (IQR 4–7) vs 8 (IQR 6–9) days; $P < 0.001$]. Delayed gastric emptying grade B/C [3 patients (6%) vs 11 patients (20%); $P = 0.04$] and endoscopic feeding tube placement [4 patients (8%) vs 14 patients (25%); $P = 0.02$] were less frequent after MIDP versus ODP. The grade B/C pancreatic fistula rate was 39% versus 23% for MIDP and ODP, respectively ($P = 0.07$) without difference in the rate of percutaneous catheter drainage for pancreatic fistula (22% vs 20%; $P = 0.77$). A Clavien–Dindo ≥III complication occurred in 13 patients (25%) after minimally invasive versus 21 patients (38%) after ODP ($P = 0.21$). No differences were found for the following complications: bleeding, surgical site infection, intensive care unit admission, surgical or radiological reintervention, and readmission. The 90-day mortality was 0% after MIDP versus 2% (n = 1) after ODP.

Minimally invasive distal pancreatectomy was associated with better overall EQ-5D-3L health utilities than ODP [mean difference adjusted for baseline scores 0.10 (95% CI 0.03–0.16, $P = 0.003$), particularly due to significant differences in EQ-5D-3L health utilities from postoperative day 3 to 30. Similarly, the overall EQ-5D-3L state of health and overall QLQ-C30 global health score were better for MIDP (Fig. 2). Detailed results on quality-of-life analysis are provided in the supplemental digital content (http://links.lww.com/SLA/B496).

Overall costs were $15,201 (95% BCaCI $12,649–$18,112) for MIDP and $17,314 (95% BCaCI $14,140–$20,706) for ODP [mean difference $−2113 (95% BCaCI $−7187 to $2762; $P = 0.41$). In a multivariable Cox regression, MIDP was independently associated with shorter time to functional recovery, as was the case for a preoperatively non-malignant tumor as indication for surgery. Details are shown in the supplemental digital content (http://links.lww.com/SLA/B496).

DISCUSSION

This first multicenter, patient-blinded, randomized controlled superiority trial demonstrated a reduced time to functional recovery after MIDP, compared with ODP. MIDP also reduced operative blood

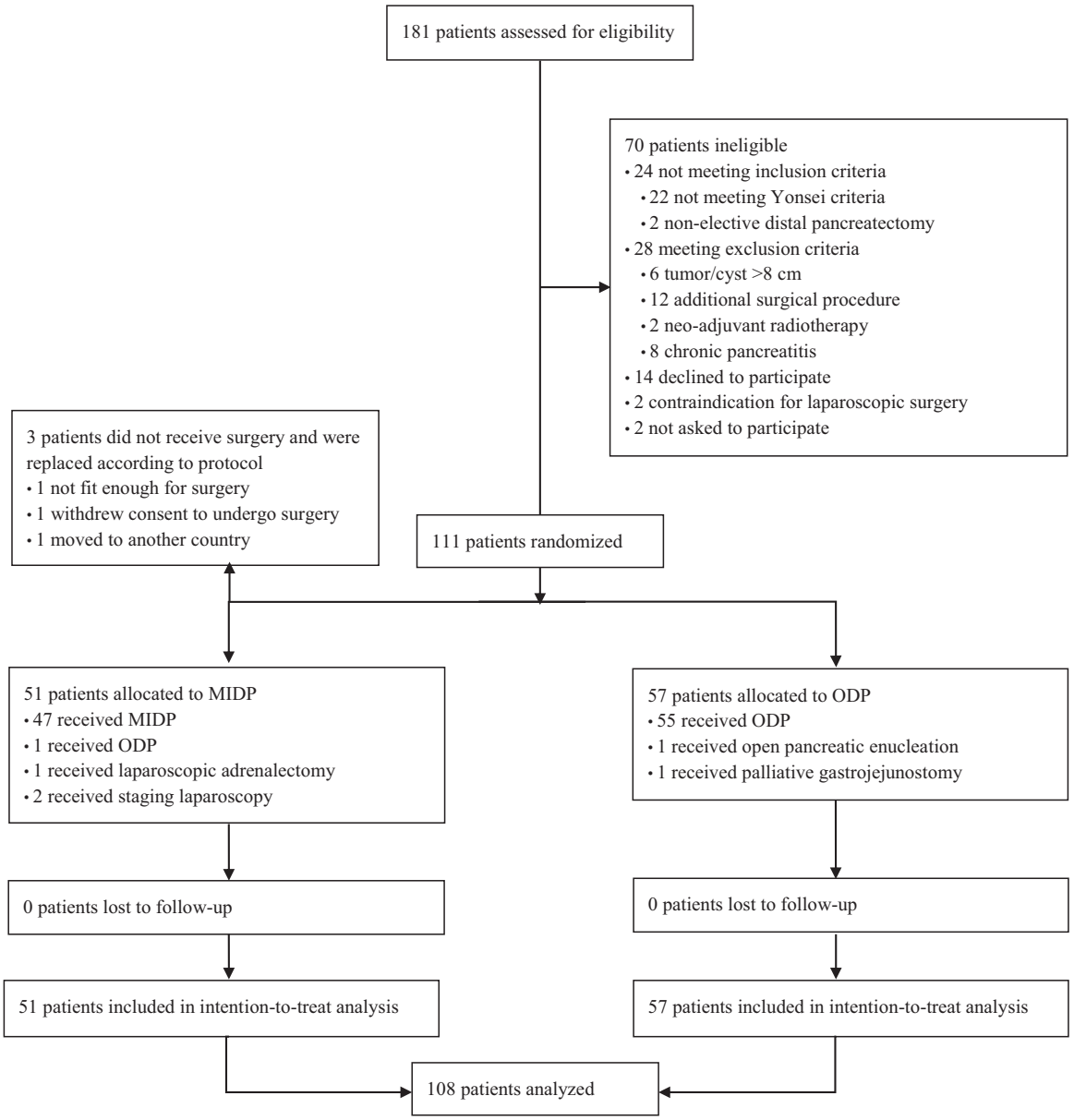

FIGURE 1. Trial profile. MIDP, minimally invasive distal pancreatectomy; ODP, open distal pancreatectomy.

loss, delayed gastric emptying, hospital stay, and impact of surgery on postoperative quality of life without increasing costs.

A systematic review of propensity score matched observational studies suggested a reduction in length of hospital stay after MIDP.[25] Most of the included studies were single-center series from expert centers which hampers their external validity. Some authors have challenged whether minimally invasive approaches can improve outcomes of open surgery in the current era of enhanced recovery after surgery programs, especially in complex procedures such as pancreatic resections.[26] Nevertheless, in this study, with enhanced recovery principles implemented in all participating centers and with most patients successfully blinded, the minimally invasive approach was able to reduce time to functional recovery from 6 to 4 days, which is a clinically relevant 33% decrease.

This study found that the rate of patients suffering from postoperative delayed gastric emptying decreased from 20% to 6% after MIDP, which translated in a reduction of (endoscopic) feeding tube placements. Delayed gastric emptying is a troublesome complication which may last for several days or even weeks and thus hampers patient recovery.[27] The rate of delayed gastric emptying in the open group was higher than previously reported[19]; this may be related to under-reporting in these retrospective studies. We also observed a trend towards an increased grade B/C pancreatic fistula rate after MIDP, although no difference in the overall need for percutaneous catheter drainage was seen. This could be explained by the finding that in the MIDP group more patients were already functionally recovered, and discharged with a surgical drain in situ, before drain amylase levels had normalized, leading to delayed drain

TABLE 1. Baseline Characteristics of Study Participants

	Minimally Invasive Distal Pancreatectomy (n = 51)	Open Distal Pancreatectomy (n = 57)	*P*
Age, mean (SD), yrs	61 (±13)	63 (±12)	0.51
Female sex	22 (43)	29 (52)	0.42
Body mass index, mean (SD) (weight, kg/height, m^2)	27 (±6)	26 (±4)	0.60
Abdominal surgery in medical history	21 (41)	27 (48)	0.52
Acute pancreatitis in medical history	3 (6)	3 (6)	>0.99
Diabetes mellitus in medical history	5 (10)	10 (18)	0.25
ASA physical status			0.57
I	13 (25)	9 (16)	
II	31 (61)	37 (66)	
III	7 (14)	10 (18)	
Tumor size on imaging, mean (SD), mm	30 (±15)	34 (±20)	0.29
Expected malignant tumor	25 (49)	30 (54)	0.71
University hospital	36 (71)	38 (67)	0.66
High-volume hospital*	22 (43)	26 (46)	0.80

*Defined as ≥10 distal pancreatectomies annually.
ASA, American Society of Anesthesiologists.

TABLE 2. Time to Functional Recovery (Primary Outcome)

	Minimally Invasive Distal Pancreatectomy (n = 51)	Open Distal Pancreatectomy (n = 57)	*P*
Time to functional recovery, median (IQR), d	4 (3–6)	6 (5–8)	<0.001
Restored mobility	4 (2–5)	5 (3–6)	0.01
Reached adequate pain control with oral medication	3 (2–3)	4 (3–5)	<0.001
Reached at least 50% required caloric intake	3 (2–5)	6 (4–7)	<0.001
No need for fluid administration	3 (2–5)	4 (3–6)	0.001
No signs of infection	4 (3–6)	6 (5–8)	<0.001

Analyzed according to intention-to-treat. All outcomes are expressed in days, as medians (IQR).
IQR, interquartile range.

TABLE 3. Intraoperative and Pathology Outcomes

	Minimally Invasive Distal Pancreatectomy (n = 51)	Open Distal Pancreatectomy (n = 57)	Relative Risk (95% CI)	*P*
Spleen-preserving procedure, n (%)	23 (45)	28 (50)	0.91 (0.64–1.31)	0.61
Kimura (splenic vessels preserving) technique	13 (25)	17 (30)		
Warshaw (splenic vessels resecting) technique	10 (20)	11 (20)		
Additional resection*	4 (8)	8 (14)	0.56 (0.18–1.75)	0.31
Operative time, median (IQR), min	217 (135–277)	179 (129–231)		0.005
Operative blood loss, median (IQR), mL	150 (50–350)	400 (200–775)		<0.001
Histopathological tumor size, mean (SD), mm	34 (±24)	34 (±19)		0.95
Histopathological diagnosis				0.58
Neuroendocrine tumor	16 (31)	22 (39)		
Pancreatic ductal adenocarcinoma	13 (25)	10 (18)		
Cystic tumor	11 (22)	20 (36)		
Pancreatitis	4 (8)	2 (4)		
Other	7 (14)	3 (5)		

Analyzed according to intention to treat. Data are expressed as mean (SD), median (IQR), or number (%).
*Additional resection besides distal pancreatectomy, splenectomy and/or adrenalectomy.
CI, confidence interval; IQR, interquartile range.

TABLE 4. Postoperative Complications

	Minimally Invasive Distal Pancreatectomy (n = 51)	Open distal Pancreatectomy (n = 57)	Relative Risk (95% CI)	*P*
Complications Clavien–Dindo grade ≥III	13 (25)	21 (38)	0.69 (0.39–1.24)	0.21
IIIa	10 (20)	15 (27)		
IIIb	1 (2)	2 (4)		
IVa	2 (4)	3 (5)		
IVb	0 (0)	2 (4)		
V	0 (0)	0 (0)		
Postoperative pancreatic fistula	20 (39)	13 (23)	1.72 (0.96–3.09)	0.07
Grade B	17 (33)	12 (21)		
Grade C	3 (6)	1 (2)		
Increased drain amylase/lipase level day 3*	28 (55)	31 (54)	1.01 (0.72–1.42)	0.96
Percutaneous catheter drainage	11 (22)	11 (20)	1.12 (0.53–2.36)	0.77
Postoperative delayed gastric emptying	3 (6)	11 (19)	0.30 (0.09–1.03)	0.04
Grade B	0 (0)	7 (13)		
Grade C	3 (6)	4 (7)		
Endoscopic feeding tube placement	4 (8)	14 (25)	0.32 (0.11–0.91)	0.02
Postoperative bleeding	2 (4)	2 (4)	1.12 (0.16–7.65)	>0.99
Grade B	2 (4)	1 (2)		
Grade C	0 (0)	1 (2)		
Endovascular coiling	0 (0)	2 (4)		0.50
Surgical re-intervention	1 (2)	3 (5)	0.37 (0.04–3.47)	0.62
Surgical site infection	2 (4)	3 (5)	0.75 (0.13–4.28)	0.74
Unplanned ICU admission	5 (10)	6 (11)	0.93 (0.30–2.87)	0.90
Length of initial hospital stay, median (IQR), d	6 (4–7)	8 (6–9)		<0.001
Readmission	15 (29)	14 (25)	1.20 (0.64–2.23)	0.57
Length of total hospital stay, median (IQR), d	6 (4–13)	8 (6–12)		0.004
Mortality	0 (0)	1 (2)		>0.99

Analyzed according to intention-to-treat. Data are expressed as median (IQR), or number (%).
*Drain amylase/lipase level higher than three times the upper level of normal serum amylase/lipase on postoperative day three.
CI, confidence interval; ICU, intensive care unit; IQR, interquartile range.

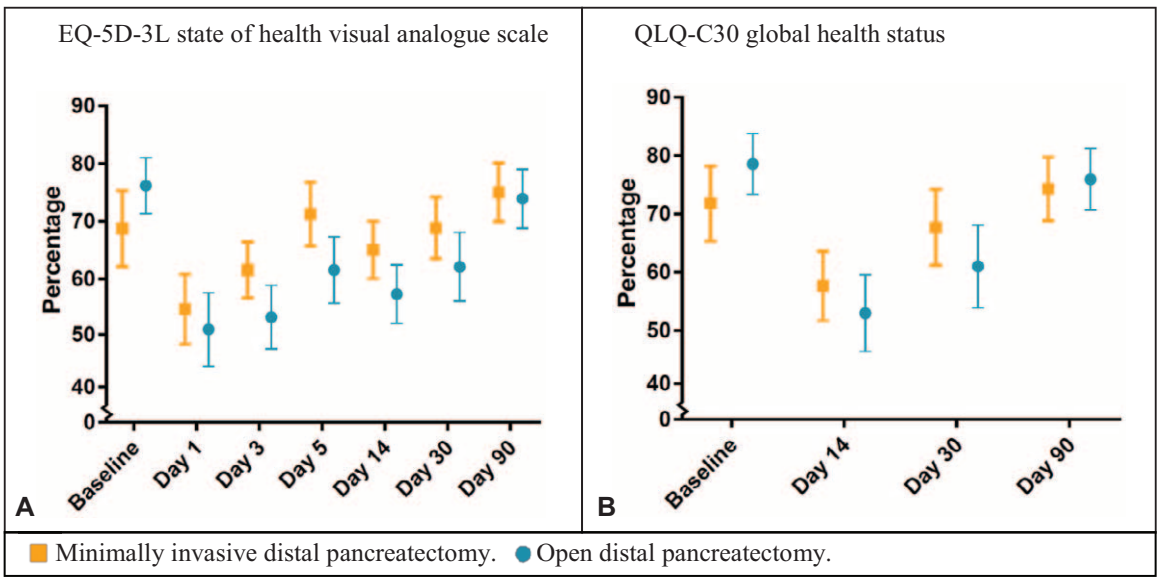

FIGURE 2. Analyzed according to intention-to-treat. Values are presented as mean quality of life scores with their 95% CI (0 indicates worst imaginable state of health, 100 indicates best imaginable state of health). The EQ-5D-3L state of health visual analogue scale overall estimated mean difference was 8 (95% CI 7.08 to 12.43, $P < 0.001$) and the QLQ-C30 global health score overall estimated mean difference 4.97 (95% CI −1.22 to 11.16, $P = 0.12$), both corrected for baseline scores. CI, confidence interval.

removal during an outpatient visit. In future practice, attention should be paid to this subgroup, as earlier outpatient visits for drain removal could reduce fistula rates and prevent prolonged patient discomfort.

Minimally invasive surgery typically increases operative costs due to the surgical instruments used and a 30-minute increased operative time. This is, however, balanced by the reduced length of hospital stay, and less delayed gastric emptying, with reduced need for endoscopic feeding tube placement, making the overall direct medial costs for MIDP comparable (ie, non-significantly less) to ODP.

The temporary decrease in quality of life was found to be significantly less after MIDP, even within the first days after surgery where patients were still blinded for received treatment. As expected, the quality of life benefit only lasted for 30 days. By then, impairment caused by surgical wounds is unlikely. Long-term follow-up—the final step of the IDEAL framework—has been started directly after trial completion to assess the full impact of MIDP on outcomes such as incisional hernia, abdominal complaints, and bowel obstruction.

A limitation of this study is that it was not designed to assess whether MIDP is superior to ODP regarding overall complications. To do so, a much larger study would be required. A second limitation of this study is that we included only a small number of patients with pancreatic ductal adenocarcinoma, which hampers the evaluation of oncological outcomes. Even though, the radical (R0) resection rate and lymph node retrieval were similar in the 23 included patients with pancreatic ductal adenocarcinoma. Future studies have to confirm the efficacy and safety of MIDP in this specific patient category.[28] A third limitation was the absence of blinding of nurses, surgeons, and researchers for treatment allocation. We cannot exclude the possibility of bias introduced by this single-blinding. However, since all patients followed the same care pathway, a large impact on outcome seems less likely. Fourth, this was a pragmatic trial leading to some variations in technique between centers and surgeons which could have influenced results. We feel that this influence was probably limited because these small variations were present for both laparoscopic and open.

A major strength of this study is its nationwide collaborative approach according to the IDEAL framework.[16–18] This study was performed only after surgeons from medium and high-volume hospitals had been trained within a structured training program. The primary endpoint was strictly defined, and patients were blinded for the intervention. Blinding in surgical randomized trials has for long been deemed impossible, although several authors emphasized the value of blinding in nonpharmacological studies to decrease bias.[29,30] Blinding proved feasible and successful in this study.

CONCLUSIONS

In conclusion, MIDP, compared with ODP, was associated with a 2-day reduction in time to functional recovery. Our results indicate that the treatment of choice for patients with left-sided pancreatic tumors is MIDP, from both a clinical and quality-of-life point of view, when performed by appropriately trained surgeons.

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