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Original Research

Stepwise implementation of laparoscopic pancreatic surgery. Case series of a single centre's experience

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ABSTRACT

Background: Laparoscopic pancreatic surgery still represents a challenge for surgeons. However, in recent decades the experience is expanding. Recent systematic reviews and meta-analyses confirm that laparoscopic pancreatic resection (LPR) is safe, feasible and worthwhile. This study analyses the first 100 consecutive LPRs in our centre.

Methods: A retrospective analysis was conducted of the first 100 LPRs in a single supra-regional Belgian centre, performed between January 2012 and January 2019. Pre-, peri- and postoperative data were retrieved from a prospectively maintained database. All procedures were performed laparoscopically by two attending surgeons, specialized in minimally invasive and hepatopancreatobiliary surgery.

Results: Of 100 procedures, 62 laparoscopic pancreatoduodenectomies (LPD) and 36 laparoscopic distal pancreatectomies (LDP) were performed, along with 1 enucleation and 1 central pancreatectomy. Indication was malignancy in 70%. Conversion rate was 24,2% in LPD and 11% in LDP. Median operative time was 330 min (IQR 300–360) in LPD and 150 min (IQR 142.5–210) in LDP. Median blood loss was 200 mL (IQR 100–487.5) in LPD and 150 mL (IQR 50–500) in LDP, transfusion rate was 22.6% and 8.3% respectively. Median length of stay (LOS) was 13 days (IQR 10–19.25) in LPD and 9 days (IQR 9–14) in LDP. R0 resection rate was 88.6% (62/70). Major complication rate (Clavien-Dindo grade III-IV) was 12%. Thirty-day mortality was 0%, 90-day mortality was 2%.

Conclusion: Our results confirm that LPR is a feasible and safe alternative to open pancreatic surgery. Safe implementation with a clear strategy is fundamental to gain experience and overcome the learning curve of this technically demanding procedures.

1. Introduction

Modern surgery is being characterized by the growing use of minimal invasive techniques. The unending endeavour to adopt them reflects technical innovations and the increasing experience of surgeons over the past 20 years. Numerous surgical procedures of diverse complexity in several domains have successfully been implemented in daily practice [1–5]. The principal advantages of minimal invasive techniques include fewer postoperative morbidities, shortened length of hospital stay (LOS) and consequently enhanced recovery to normal functioning [6].

Pancreatic surgery runs a lagging course in this evolution. It is traditionally considered to be demanding and requires high expertise. Intra-operative technical challenges are primarily due to the organ's retroperitoneal position with proximity to important vascular structures. This requires a complex dissection that is often modified by reason of anatomical variations. Additionally, a thorough preoperative workup and postoperative alertness for possible hazardous complications are as important to reduce morbidity and mortality.

Despite these challenges a natural drive remains towards further development of minimally invasive approaches in pancreatic resection. The role of laparoscopic pancreatic surgery has extended from a diagnostic tool in the early 1990s to complex resections in malignant disease with lymphadenectomy [6–8].

Recent systematic reviews and meta-analyses confirm that minimally invasive pancreatic resection (MIPR) is safe, feasible and worthwhile [6,9–12]. Some reports suggest possible advantages of MIPR on the overall morbidity rate compared with open pancreatic

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Abbreviations

MIPR	minimally invasive pancreatic resection
OPR	open pancreatic resection
ISGPS	International Study Group of Pancreatic Surgery
DGE	delayed gastric emptying
POPF	postoperative pancreatic fistula
LPD	laparoscopic pancreatoduodenectomy
LDP	laparoscopic distal pancreatectomy
SMV	Superior mesenteric vein
IQR	interquartile range
PJ	pancreatojejunostomy
LOS	length of hospital stay

resection (OPR) [9,13]. However, these results are mainly based on retrospective data and lack long-term oncological follow-up results. Randomized data has only found entrance in this domain in the last 3 years, with miscellaneous results thus far [13–16].

2. Methods

A retrospective analysis of the first 100 laparoscopic pancreatic resections performed between 2012 and January 2019 was conducted from a prospectively collected database in a single supra-regional Belgian centre.

Surgery was performed by two attending surgeons, specialized in laparoscopic and pancreatic surgery. The surgical experience of both surgeons before implementation of MIPR in our centre was respectively > 120 and > 70 OPRs. In addition, it was preceded by observational visits to the vastly experienced innovator in MIPR, Dr. M. Kendrick, M.D. (Mayo Clinic, Rochester, Minnesota). The key technical aspects of these surgical approaches were learned during yearly visits between 2007 and 2012.

Indications for resection were both benign and malignant. All patients of ≥18 years old diagnosed with suspect lesions located in the pancreas, ampulla, duodenum or distal bile duct were presented in the multidisciplinary oncological team. In case of biopsy-proven malignancy or clinical and radiological suspicion without confirmed malignancy, surgical resection was considered, in accordance with oncological standards [17]. Selective criteria determined the choice for the laparoscopic approach: small tumours (< 35 mm), T1/T2 tumours or non-PDAC tumours. Exclusion criteria where neoadjuvant radiotherapy, involvement of major vessels on preoperative imaging. Furthermore, history of chronic pancreatitis and morbid obesity were also taken into account, without defined exclusion criteria. For tumours located in the pancreatic body or tail, the Yonsei criteria were applied [18].

Diagnostic laparoscopy was routinely performed in malignant cases proposed for resection, to exclude peritoneal carcinomatosis, since diagnostic accuracy is higher than imaging by CT or MRI. Additionally, accurate determination of resectability and eligibility for a laparoscopic approach was achieved during this diagnostic laparoscopy using intraoperative ultrasound [19].

The Clavien-Dindo classification was used for morbidity classification [20]. The International Study Group of Pancreatic Surgery (ISGPS) recommendations for grading delayed gastric emptying (DGE) and postoperative pancreatic fistula (POPF) were utilized for description of these complications [21,22]. The study was approved by the local ethics committee (B396201940175).

This paper has been reported in line with the PROCESS criteria for case series [23].

Pre-, peri- and postoperative data were retrieved from a prospectively maintained electronic database. Short-term follow-up consisted of a routine outpatient control by the operating surgeon 4 weeks after discharge. Additional outpatient consultations were planned according to clinical necessity. Mid- and long-term oncological follow-up data was collected through the local patient file system and regional clinical network platform.

Descriptive statistical analysis was conducted with SPSS Statistics 25 software (SPSS, Inc., Chicago, Illinois).

2.1. Technique of laparoscopic pancreatoduodenectomy (LPD)

The technical approach of LPD is largely based on the technique described by Kendrick et al. [24]. Six trocars are placed largely in a line to adequately approach the pancreas and liver hilum. The dissection starts with exposure of the lesser sac by division of the gastrocolic ligament. Kocher manoeuvre is performed after mobilisation of the hepatic colic flexure. A tunnel is dissected at the posterior side of the pancreatic neck at the level of the superior mesenteric vein (SMV), identified at the inferior border. Nylon tape is placed to encircle the pancreatic neck for identification and to lift it up. Dissection and ligation of the gastroduodenal artery and right gastric artery is performed and subsequently a 60 mm Echelon™ stapler (Ethicon, Inc., Bridgewater, New Jersey) transects the duodenum 2 cm distal to the pylorus. Cholecystectomy is performed, followed by ligation and transection of the common bile duct. The proximal jejunum is mobilised and transected 15 cm distal to the ligament of Treitz with a 60 mm stapler. The pancreatic neck is then divided using electrocautery or ultrasonic shears. Further dissection of the pancreatic head from the retroperitoneum is performed with attention for tributary branches. The specimen is placed in an endobag and extracted through an extended infra-umbilical trocar site.

Reconstruction was performed with a two-layer end-to-side pancreatojejunostomy (PJ), preferably duct-to- mucosa anastomosis. In case of indistinct pancreatic duct or soft pancreas, a dunking anastomosis was performed. The outer layer was generally sewn with 4/0 polyglycolic acid suture Vicryl® (Ethicon, Inc., Bridgewater, New Jersey). We recently modified the suturing material of the PJ. In the most recent cases, both anastomoses currently consist of an outer layer sewn with non-absorbable running 3/0 V-loc™ barbed suture (Medtronic, Inc., Fridley, Minnesota), as illustrated in Fig. 1. The

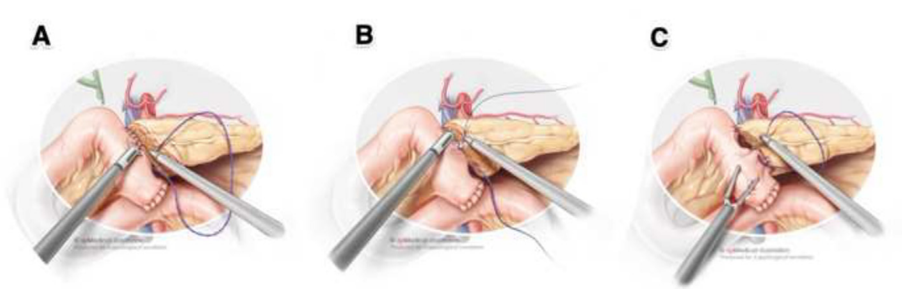

Fig. 1. Illustration of the 2 types of pancreatojejunostomy anastomoses: A. Posterior layer sewn with running V-loc™ 3/0 suture. This is applied in both anastomosis types. B. Duct-to-mucosa anastomosis layer with interrupted 5/0 monofilament sutures over a fine gastric tube that is inserted in the pancreatic duct. C. Anterior layer sewn with running V-Loc™ 3/0 suture in the dunking anastomosis.

pancreatic duct in the duct-to-mucosa anastomosis is sewn to the jejunal stump over a fine gastric tube with 5/0 absorbable monofilament Maxon™ (Medtronic, Inc., Fridley, Minnesota). Diameter of the gastric tube varies from 3.5 to 8 French, depending on the diameter of the pancreatic duct.

An end-to-side hepaticojejunostomy was standardly performed with running or interrupted polyglycolic acid sutures Vicryl® (Ethicon, Inc., Bridgewater, New Jersey). In dilated hepatic ducts, we introduced resorbable running 3/0 V-loc™ barbed suture (Medtronic, Inc., Fridley, Minnesota).

Dissection was commonly performed with bipolar cautery devices and advanced energy shears Enseal® (Ethicon, Inc., Bridgewater, New Jersey) or LigaSure™ (Medtronic, Inc., Fridley, Minnesota). Two indwelling low suction silicone drainage catheters were routinely placed, on the anterior and posterior side of the pancreato- and hepaticojejunostomy.

2.2. Technique of laparoscopic distal pancreatectomy (LDP)

LDP was generally performed in a 'medial-to-lateral' approach. Dissection is started with division of the gastrocolic ligament and entrance of the lesser sac. The SMV is identified at the inferior border of the pancreas. The SMV is dissected from the pancreatic body and a tunnel is created posteriorly of the pancreatic body. After encircling with nylon tape, the pancreas is lifted and a 60 mm Echelon™ stapler (Ethicon, Inc., Bridgewater, New Jersey) is used for pancreas transection. Subsequently dissection from the retroperitoneum towards the tail of the pancreas is performed using electrocautery or Ligasure™ device (Medtronic, Inc., Fridley, Minnesota). Attention is given to ligation of small branches of the splenic artery near the pancreatic tail. The specimen is retracted and one indwelling low suction silicone drainage catheter was routinely placed in the lesser sac.

In malignant disease distal pancreatectomy is combined with splenectomy to provide a sufficient lymphadenectomy along the splenic artery and hilum. In benign disease preservation of the spleen is recommended, as it is associated with a reduction of postoperative infection rate [25]. We prefer to apply the Kimura technique, which involves full preservation of de splenic artery and vein to prevent postoperative splenic infarction [26].

3. Results

Of 100 procedures, 62 LPDs and 36 LDPs were performed, along with 1 enucleation and 1 central pancreatectomy. Patient characteristics can be found in Table 1. Median age at the time of resection was 69 years. Peri-operative data of the LPD and LDP groups are described in Table 2. Comorbidities were present preoperatively in 61%.

Malignancy was proven histopathologically in 70%. The detailed pathological findings of LDP and LDP groups can be found in Table 3. One pancreatic enucleation was performed for a small neuro-endocrine tumour, located in the uncinate process. A central pancreatectomy was indicated for a cystic lesion in the pancreatic body. Histopathologically an IPMN was detected.

R0 resection was considered when the tumour free margins were > 1 mm. This was achieved in 62 of 70 malignant cases (88.6%). Major morbidity rate (Clavien-Dindo III-IV) was 12%. Overall 30-mortality was 0% and 90-day mortality was 2%.

3.1. Laparoscopic pancreatoduodenectomy

Table 2 illustrates the peri- and postoperative characteristics. Sixty-two LPDs were performed, with median operation time of 330 min (IQR 300–360). Estimated median blood loss was 200 cc (IQR 100–487.5), conversion rate was 24,2%. Reason for conversion was bleeding in 4 patients and peripancreatic fibrosis in 5 patients. Other reasons were aberrant anatomy, obesity and tumour adherence to the portal vein.

One portal vein resection (1.6%) was required. Pancreatojejunostomy was performed with duct-to- mucosa anastomosis in 42 cases (67.7%). In all other cases a dunking anastomosis was performed (32.3%). The median diameter of the pancreatic duct was 4.0 mm.

Postoperative complications occurred in 44 patients (71.0%), with Clavien-Dindo ≥ III in 10 (16.1%). Peri- and postoperative blood cell transfusion was administered in 14 patients (22.6%), including 4 patients who received blood during the procedure. Nineteen patients (30.6%) developed a postoperative pancreatic fistula (POPF), of whom 6 (9.7%) had grade B POPF, and 2 (3.2%) had grade C POPF, according to the ISGPS grading system [22]. One patient died from the complications of the combination of a grade C POPF with catheter sepsis. Clinically relevant postoperative haemorrhage occurred in 5 patients (8.1%), and two (3.2%) of these received an urgent percutaneous transcatheter embolisation. Five patients (8.1%) had a revision procedure, in 1 case a laparoscopy was sufficient. Median LOS was 13 days (IQR 10–19.25).

3.2. Laparoscopic distal pancreatectomy

Table 2 illustrates the peri- and postoperative characteristics. A total of 36 LDPs were performed. Median operating time was 150 min (IQR 142.5–210), median estimated blood loss was 150 cc (IQR 50–500), conversion rate was 11%. Reason for conversion was bleeding in 2 patients and tumour adherence to the colon mesentery in 2 other cases. One portal vein resection (2.8%) was performed.

Postoperative complications occurred in 21 patients (58.3%). Major complications (Clavien-Dindo ≥

III) were present in only 5 patients (13.9%). One patient had respiratory failure with prolonged intubation (Grade IVa). One patient had haemorrhagic shock, based on sudden, but severe varicosal bleeding in the duodenum. Evolution to hepatic failure and fatal multi-organ failure (Grade V). Blood cell transfusion was administered in 3 patients (8.3%), none were given intra-operatively. Fifteen POPFs were listed, among which 2 patients with grade B POPF (5.6%) and 2 with grade C POPF (5.6%). DGE grade A occurred in 1 patient (2.8%). No relevant haemorrhages occurred. One exploratory laparoscopy (2.8%) was performed in the patient with varicosal duodenal bleeding.

Median LOS was 9 days (IQR 9–14).

4. Discussion

This paper describes the experience of the first 100 minimal invasive pancreatic resections in our supra-regional centre. The majority of the procedures (62%) were LPDs, along with 36 LDPs, one pancreatic enucleation and one central pancreatectomy. Since these procedures have different technical aspects and indications, they have been considered separately in the following discussion.

Table 1
Patient preoperative characteristics.

Patient characteristic	LPD	LDP	Total
	N = 62	N = 36	N = 100
Sex (M:F)	31:31	22:14	46:54
Age at surgery, median	70	68	69
ASA score, mean	1.85	1.97	1.88
Preoperative BMI, median	24.61	25.12	24.61
Smoking (%)	11 (17.7)	6 (16.7)	17
Alcohol abuse (%)	7 (11.3)	0	7
Comorbidities (%)	39 (62.9)	22 (61.1)	61

Table 2
Peri- and postoperative characteristics of the LPD and LDP group. The central pancreatectomy and pancreatic enucleation are not included in this table.

Peri- and Postoperative Characteristic	LPD	LDP
	N = 62	N = 36
Duration of surgery (mins), median (IQR)	330 (300–360)	150 (142.5–210)
Blood loss (mL), median (IQR)	200 (100–487.5)	150 (50–500)
Conversion (%)	15 (24.2)	4 (11)
Transfusion need (%)	14 (22.6)	3 (8.3)
Spleen preservation (%)	–	7 (19.4)
Portal vein resection (%)	1 (1.6)	1 (2.8)
Diameter pancreatic duct (mm), median (IQR)	4.0 (2.0–6.0)	–
Pancreaticojejunostomy type (%)		
Duct-to-mucosa	42 (67.7)	–
Dunking	20 (32.3)	–
Postoperative complications (%)	44 (71)	21 (58.3)
Clavien-Dindo (%)		
Grade I-II	34 (54.8)	15 (41.7)
Grade III	9 (14.6)	3 (8.4)
Grade IV	–	1 (2.8)
Grade V	1 (1.6)	1 (2.8)
POPF (%) – ISGPS	19 (30.6)	15 (41.7)
Grade A	10 (16.6)	11 (30.6)
Grade B	6 (9.7)	2 (5.6)
Grade C	2 (3.2)	2 (5.6)
DGE (%) – ISGPS	13 (21%)	1 (2.8)
Grade A	12 (19.4)	1 (2.8)
Grade B	1 (1.6)	–
Grade C	–	–
Post-pancreatectomy haemorrhage	5 (8.1)	–
Embolisation	2 (3.2)	–
Surgical site infections (%)	2 (3.2)	1 (2.8)
Revision laparotomy (%)	4 (6.5)	–
Relaparoscopy (%)	1 (1.6)	1 (2.8)
Length of stay (days), median (IQR)	13 (10–19.25)	9 (9–14)

Table 3
Overview of the indications, pathological outcomes and short-term mortality. (*): 1 central pancreatectomy and 1 pancreatic enucleation are not included in this table.

Pathology and survival characteristics	LPD	LDP	Total*
Pathological diagnosis	N = 62	N = 36	N = 100
Malign (%)	50 (80.6)	19 (52.8)	70*
Adenocarcinoma	46	13	59
Pancreas	29	13	42
Ampulla	10	–	10
Duodenum	4	–	4
Common bile duct	3	–	3
Neuro-endocrine carcinoma	4	4	9
Solitary metastasis	–	1	1
Invasive IPMN	–	1	1
Benign	12 (19.4)	17 (47.2)	30*
IPMN	4	4	9
Serous (micro)cystic adenoma	–	3	3
Mucinous (cyst)adenoma	1	3	4
Pancreatitis	3	4	7
Other	4	3	7
N harvested lymph nodes, median (IQR)	10 (7–12.5)	3.5 (6)	
Maximal diameter tumor (mm), median (IQR)	25 (18–35)	33.5 (22–44)	
R0 resection (%)	43/50 (86)	18/19 (94.7)	62/70 (88.6)
30-day mortality	0	0	0
90-day mortality	1	1	2

4.1. Laparoscopic pancreatoduodenectomy

Pancreatoduodenectomy remains associated with high postoperative comorbidity rates. The tempered enthusiasm for a minimal invasive approach of this procedure is mainly attributed to the technical demanding issues.

Moreover, the exclusively retrospective data of the last two decades cannot easily reproduce results that show a clear benefit of performing LPD over OPD [27,28]. The experience and evidence of LPD is growing increasingly, including the first published randomized controlled trials [13–15].

A sufficient number of comparative studies confirm the feasibility and safety of LPD [13,14,29–33]. Comparison of our results of LPD with the available data show that these are largely in line with these findings. Meta-analysis of non-randomized comparative studies indicate a significant reduction in estimated blood loss, postoperative haemorrhage, transfusion rate and wound infection associated with LPD in comparison to OPD [6]. These reports show no significant differences in POPF, DGE and bile leakage. In addition, the PADULAP randomized trial notes a significantly lower major complication rate (Clavien-Dindo ≥ III) in the LPD group [13]. In our series, severe postoperative complications (Clavien-Dindo grade ≥ III) were present in 16.2%, with clinically important POPF (grade B–C) in 8 patients (12.9%), and only 1 patient with DGE (grade B).

Palanivelu et al. randomized 64 patients with periampullary tumours to either LPD or OPD. They noted a significant reduction in LOS in de LPD group. The overall complication rate was similar [14]. The PADULAP trial confirmed this significant shorter LOS. However, significant longer operative times were needed for the laparoscopic approach [13].

The most recently published LEOPARD-2 trial reported some worrisome results. The group of Besselink noted a significantly higher complication-related mortality rate in de LPD group (LPD 10% vs OPD 2%, RR 4.90) and were forced to terminate the trial prematurely for this reason. Major complication rate and functional recovery were comparable between groups [15].

Our analysis was partly performed in the context of the worrisome results of the LEOPARD-2 trial. Our short-term mortality rate is acceptable, with none at 30 days and 1 case described above at 90 days. Along with our major complication rate (16.1%) and conversion rate (24.2%), we considered our first experience as feasible and safe. Matched comparison of LPD and OPD is the next step in validation of our results.

Besides, the Belgian Federal Government recently started with centralisation of pancreatic surgery. Since July 2019 our centre, along with 14 other centres, is recognized as reference centre for pancreatic surgery in Belgium. The Federal Government strictly monitors the peri- and postoperative results and short-term follow-up results (90-days) per centre. Re-evaluation is planned after 3 years, with reallocation of the reference centres.

We recently modified our PJ technique, by using the polybutester V-loc™ 3/0 barbed suture (Medtronic, Inc., Fridley, Minnesota) in the outer layer, instead of polyglycolic acid sutures. Since a few years, attention has been given to the suturing material, used in this difficult anastomosis. Studies are being conducted to compare different surgical strategies of the PJ, in an attempt to minimize the burden of POPFs. The role of suture material on the rate of POPF is not entirely clear yet. It is believed that pancreatic juice and bile may have harmful effects on the suturing material and give mechanical dehiscence. The Verona group recently published a propensity score-matched comparison of polydioxanone and polyester sutures in PJ. Their risk-adjusted analysis illustrates a significant lower POPF rate ($p = 0.02$), when PJ was performed with polyester sutures [34]. A possible additional effect of a barbed polyester suture is the distributed tension over the length of the suture, which allows application in soft pancreatic tissue.

The clinically relevant POPF rate in our LPD series is acceptable with 12.9%. We believe this suture choice can improve our results in the future.

Negative margins (R0) were achieved in 86% in our series. Two meta-analyses suggest that LPD tends to have higher R0 resection rate and more lymph nodes harvested [6,35]. This could be interpreted as an advantage of the magnified view during laparoscopy. It is suggested that the tumour size of LPD groups is - although often not significantly-smaller compared to OPD groups. In our series we selected patients with small tumours (< 35 mm), T1/T2 tumours and non-PDAC tumours for laparoscopic approach. This could indicate a potential bias that may account for the higher R0 resection rates. However, the first randomized studies note similar tumour sizes, lymph node harvests and R0 resection rates [13,36].

Regarding resection margins, a possible bias must be considered, because definitions of R0 resection differ in the literature [37]. Pathologists in our centre concluded to R0 resection when > 1 mm tumour free margin was achieved. Standardization is required to avoid incorrect interpretation of this oncological outcome.

4.2. Laparoscopic distal pancreatectomy

LDP has gained popularity among gastrointestinal surgeons because the procedure does not require anastomosis or other reconstruction and presents fewer challenges than pancreatoduodenectomy.

Similarly to LPD, the literature of LDP exclusively consisted of retrospective comparative studies until recently. This data demonstrates the growing experience, safety and feasibility of performing LDP in both malignant and benign pathologies [7,38–40]. Oncologic outcomes between LDP and ODP performed for malignancy appear similar as well, but these data are limited [39,41].

Results of a recent meta-analysis indicate that LDP did not adversely affect long-term survival in PDAC patients [39]. In addition, this non-randomized data suggests a possible advantage of LDP, in terms of estimated blood loss, complication rate, shorter LOS, and oncological outcomes [39,42]. The presumed oncological advantage is, similarly to LPD, mainly based on significant higher R0 resection rates and non-significant larger number of harvested lymph nodes [39]. These possible advantages must be interpreted with caution, since these analyses exclusively contain non-randomized studies. Again, randomized trials with long-term oncological outcomes are required to validate these presumptions.

To date, the LEOPARD-trial is the solitary randomized controlled trial comparing LDP and ODP, with attention to functional recovery. It confirmed a significant shorter time to functional recovery in LDP, with a comparable overall complication rate in the two groups [16]. These are auspicious results that need to be validated by more randomized data.

Compared with the available evidence, the results of our series of LDP are in line in terms of perioperative parameters and postoperative complications.

4.3. Implementation of minimal invasive pancreatic surgery

Considering the technically demanding character of pancreatic surgery, with therefore a steep learning curve, attention was given to safely implement this approach. Today our team consists of two attending surgeons with large experience with pancreatic surgery and laparoscopic techniques. The implementation of both LDP and LPD was introduced in 2012. The early phase of implementation leaned on the experience of one senior surgeon (F.V.), considered "pioneer", according to the IDEAL framework [41]. The second HPB surgeon (M.D.) was trained by the senior attending and can be considered "early adopter" [43].

The implementation of LPD in our center was preceded by gaining understanding of this approach from M. Kendrick, M.D. (Mayo Clinic, Rochester, Minnesota), who published on LPD as an innovator [24]. Since 2007, annual observational visits provided crucial insights of the peri- and postoperative aspects of LPD. At the start of implementation in 2012, hepatopancreatobiliary surgical pathology was temporarily split up in the team, allowing one surgeon to focus on LPD and one surgeon on complex laparoscopic liver surgery. This created higher volumes per surgeon per surgical pathology and shortened the learning curve in time.

Studies suggest that 30 to 40 procedures are required to overcome the learning curve of LPD [44,45]. The experience was passed on from pioneer to early adopter after performance of 45 cases by the pioneer. From that moment all procedures were performed with both surgeons at the operating table. This strategy provides a minimizing learning curve for the early adopter and increases the safety of implementation.

Analysis of the first procedures shows that these were immediately performed for malignant indications. In fact, the first 8 LPDs performed were all pancreatic ductal adenocarcinomas. Comparison of the first 10 and last 10 LPDs shows a shorter median duration of the procedure of 50 min in the last 10 LPDs (387.5min vs 337.5min). This suggests a favorable evolution in our learning curve. Postoperative complication rate, median LOS and tumour diameter were comparable between this early and recent groups.

LDPs were routinely performed by both surgeons by oneself. No measures were taken to overcome any learning curve for this procedure, which is substantially less complex than LPD. The learning curve for LDP seems to be considerably shorter than for LPD, suggested as few as 10 to 17 cases [46–48]. These were relatively small studies. The study group of Southampton, however, advocated that the learning curve is overcome after 30 performed LDPs, since a signification reduction of postoperative complications (Clavien-Dindo ≥ III) from 30% to 5% was seen after 30 cases performed [49].

4.4. Limitations

The first important limitation is that this series of MIPR consists of both distal pancreatectomy and pancreatoduodenectomy, along with one pancreatic enucleation and one central pancreatectomy.

These are separate entities with their own characteristics, especially regarding technical performance. Moreover, all indications are combined in this analysis.

Secondly, this study was conducted in a retrospective manner with only short-term follow-up data thus far. Data is being prospectively maintained further and consequently long-term outcomes are on their way. Our intention is to perform a comparative study between LPD and OPD through propensity score-matching, which is believed to provide valuable and timely insights in the absence of a randomized study design [38].

Nevertheless, more randomized controlled trials are required to validate clear advantages of MIPR over OPR. The results of the LEOPARD-2 trial can't be ignored and emphasize the potential hazardous complications, associated with pancreatic surgery. OPR will remain present, regardless of a growing place for MIPR. Resection of a tumour with vascular involvement of the mesenteric axis considerably increases the technical complexity and risk for major bleeding. Few studies are available describing major vessel reconstruction during MIPR [50,51]. This requires advanced laparoscopic skills to complete such procedures safely. It is not justified to implement major vessel reconstruction in routine practice yet.

5. Conclusion

Implementation of LPD and LDP in our centre was feasible and safe. A stepwise strategy from innovator to pioneer to early adopter allowed shortening of the learning curve. The added value of MIPR over OPR is put forward, but is waiting to be confirmed with randomized clinical trials and robust prospective comparative studies.

Ethical approval

The study was approved by the local ethics committee (B396201940175).

Sources of funding

None.

Author contribution

Mathieu Vandeputte: Conceptualization; Data curation; Formal analysis; Methodology; Resources; Software; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.

Mathieu D'Hondt: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Roles/Writing - original draft; Writing - review & editing.

Edward Willems: Data curation; Investigation.

Celine Demeyere: Data curation; Formal analysis; Investigation.

Isabelle Parmentier: Data curation; Formal analysis; Investigation.

Franky Vansteenkiste: Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing - review & editing.

All authors meet all 4 criteria of the International *Committee of Medical Journal Editors (ICMJE) guidelines*.

Research registration number

Name of the registry: *Researchregistry.com*.

Unique Identifying number or registration ID: *researchregistry5074*.

Hyperlink to the registration (must be publicly accessible):

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Mathieu D'Hondt (Corresponding Author).

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Statement of ethics

The study was approved by the local ethics committee (B396201940175).

This article was written in accordance with the ethical standards of the institutional review board and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all human subjects as is the standard of care and as with compliance with institution guidelines.

This study is registered with the ResearchRegistry and the unique identifying number is: researchregistry5074.

Declaration of competing interest

The authors declare that they have no conflict of interest.

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Appendix A. Supplementary data

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References

[1] I. Abraha, G.A. Binda, A. Montedori, A. Arezzo, R. Cirocchi, Laparoscopic versus Open Resection for Sigmoid Diverticulitis, [Internet], Cochrane Database Syst Rev (2017 Nov 25) Available from https://doi.org/10.1002/14651858.CD009277.pub2.

[2] M. D'Hondt, E. Tamby, I. Boscart, S. Turcotte, I. Parmentier, H. Pottel, et al., Laparoscopic versus open parenchymal preserving liver resections in the posterosuperior segments: a case-matched study, Surg. Endosc. 32 (3) (2018 Mar) 1478–1485.

[3] R.H. Kennedy, E.A. Francis, R. Wharton, J.M. Blazeby, P. Quirke, N.P. West, et al., Multicenter randomized controlled trial of conventional versus laparoscopic surgery for colorectal cancer within an enhanced recovery programme: EnROL, [Internet], J Clin Oncol 32 (17) (2014 Jun 10) 1804–11. Available from: http://ascopubs.org/doi/10.1200/JCO.2013.54.3694.

[4] J.Y. You, H.Y. Kim, Y.J. Chai, H.K. Kim, A. Anuwong, R.P. Tufano, et al., Transoral robotic thyroidectomy versus conventional open thyroidectomy: comparative analysis of surgical outcomes in thyroid malignancies, J Laparoendosc Adv Surg Tech 29 (6) (2019) 796–800 https://www.liebertpub.com/doi/10.1089/lap.2018.0587.

[5] H. Long, Q. Tan, Q. Luo, Z. Wang, G. Jiang, D. Situ, et al., Thoracoscopic surgery versus thoracotomy for lung cancer: short-term outcomes of a randomized trial, [Internet], Ann Thorac Surg 105 (2) (2018 Feb) 386–392. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0003497517311918.

[6] S. Wang, N. Shi, L. You, M. Dai, Y. Zhao, Minimally invasive surgical approach versus open procedure for pancreaticoduodenectomy: a systematic review and meta-analysis, Med (United States). 96 (50) (2017).

[7] M.A. Hilal, A.S. Takhar, Laparoscopic left pancreatectomy: current concepts, [Internet], Pancreatology 13 (4) (2013) 443–448, https://doi.org/10.1016/j.pan.2013.04.196 Available from:.

[8] C.M. Vollmer, H.J. Asbun, J. Barkun, M.G. Besselink, U. Boggi, K.C.P. Conlon, et al., Proceedings of the first international state-of-the-art conference on minimally-invasive pancreatic resection (MIPR), [Internet], Hpb 19 (3) (2017) 171–177, https://doi.org/10.1016/j.hpb.2017.01.015 Available from:.

[9] M. Cesaretti, L. Bifulco, R. Costi, A. Zarzavadjian Le Bian, Pancreatic resection in the era of laparoscopy: state of Art. A systematic review, [Internet], Int J Surg 44 (2017) 309–316, https://doi.org/10.1016/j.ijsu.2017.07.028 Available from:.

[10] F. Guerra, G. Giuliani, L. Bencini, P.P. Bianchi, A. Coratti, Minimally invasive versus open pancreatic enucleation. Systematic review and meta-analysis of surgical outcomes, J. Surg. Oncol. 117 (7) (2018) 1509–1516.

[11] K. Chen, Y. Pan, X long Liu, G yi Jiang, D. Wu, H. Maher, et al., Minimally invasive pancreaticoduodenectomy for periampullary disease: a comprehensive review of literature and meta-analysis of outcomes compared with open surgery, BMC Gastroenterol. 17 (1) (2017) 1–15.

[12] S.R. Coles, M.G. Besselink, K.R. Serin, H. Alsaati, P. Di Gioia, M. Samim, et al., Total laparoscopic management of lesions involving liver segment 7, [Internet], Surg Endosc Other Interv Tech 29 (11) (2015), https://doi.org/10.1007/s00464-014-4052-2 3190–5. Available from:.

[13] I. Poves, F. Burdío, O. Morató, M. Iglesias, A. Radosevic, L. Ilzarbe, et al., Comparison of perioperative outcomes between laparoscopic and open approach for Pancreatoduodenectomy: : the PADULAP randomized controlled trial, [Internet], Ann Surg 268 (5) (2018 Nov) 731–739. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30138162.

[14] C. Palanivelu, P. Senthilnathan, S.C. Sabnis, N.S. Babu, S. Srivatsan Gurumurthy, N. Anand Vijai, et al., Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours, Br. J. Surg. 104 (11) (2017) 1443–1450.

[15] J. van Hilst, T. de Rooij, K. Bosscha, D.J. Brinkman, S. van Dieren, M.G. Dijkgraaf, et al., Laparoscopic versus open pancreatoduodenectomy for pancreatic or periampullary tumours (LEOPARD-2): a multicentre, patient-blinded, randomised controlled phase 2/3 trial, Lancet Gastroenterol Hepatol 4 (3) (2019) 199–207, https://doi.org/10.1016/S2468-1253(19)30004-4 http://www.ncbi.nlm.nih.gov/pubmed/30685489.

[16] T. de Rooij, J. van Hilst, H. van Santvoort, D. Boerma, P. van den Boezem, F. Daams, et al., Minimally invasive versus open distal pancreatectomy (LEOPARD): a multicenter patient-blinded randomized controlled trial, [Internet], Ann Surg 269 (1) (2019 Jan) 2–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30080726.

[17] M. Ducreux, A. Sa Cuhna, C. Caramella, A. Hollebecque, P. Burtin, D. Goéré, et al., Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up †, [Internet], Ann Oncol 26 (2015) 56–68. Available from: https://academic.oup.com/annonc/article-abstract/26/suppl_5/v56/344501.

[18] S.H. Lee, C.M. Kang, H.K. Hwang, S.H. Choi, W.J. Lee, H.S. Chi, Minimally invasive RAMPS in well-selected left-sided pancreatic cancer within Yonsei criteria: long-term (> median 3 years) oncologic outcomes, [Internet], Surg Endosc 28 (10) (2014 Oct 23) 2848–55. Available from: http://link.springer.com/10.1007/s00464-014-3537-3.

[19] R.E. Jimenez, A.L. Warshaw, C. Fernandez-Del Castillo, Laparoscopy and peritoneal cytology in the staging of pancreatic cancer, [Internet], J Hepatobiliary Pancreat Surg 7 (1) (2000) 15–20. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10982586.

[20] P.A.1 Clavien, J. Barkun, M.L. de Oliveira, J.N. Vauthey, D. Dindo, R.D. Schulick, E. de Santibañes, J. Pekolj, K. Slankamenac, C. Bassi, R. Graf, R. Vonlanthen, R. Padbury, J.L.M.M. Cameron, The Clavien-Dindo classification of surgical complications: five-year experience, Ann. Surg. 250 (2) (2009) 187–196.

[21] D.J. Gouma, L.W. Traverso, A. Fingerhut, M.N. Wente, M.G. Sarr, C. Dervenis, et al., Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS), [Internet], Surgery 142 (5) (2007) 761–768. Available from: https://ac.els-cdn.com/S0039606007003017/1-s2.0-S0039606007003017-main.pdf?_tid=a224e3c7-45a6-4e9e-8f89-c7eb7d8c0342&acdnat=1550999261_6964f5526925a5af21be993f19afc59d.

[22] C. Bassi, G. Marchegiani, C. Dervenis, M. Sarr, M. Abu Hilal, M. Adham, et al., Pancreas the 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years after, [Internet], Surgery 161 (2017) 584–591, https://doi.org/10.1016/j.surg.2016.11.014 Available from:.

[23] R.A. Agha, M.R. Borrelli, R. Farwana, K. Koshy, A.J. Fowler, D.P. Orgill, et al., The PROCESS 2018 statement: updating consensus preferred reporting of CasE series in surgery (PROCESS) guidelines, Int J Surg (60) (2018) 279–282 https://www.sciencedirect.com/science/article/abs/pii/S1743919118316777.

[24] M.L. Kendrick, D. Cusati, Total laparoscopic pancreaticoduodenectomy: feasibility and outcome in an early experience, [Internet], Arch Surg 145 (1) (2010 Jan 1) 19–23. Available from: http://archsurg.jamanetwork.com/article.aspx?doi=10.1001/archsurg.2009.243.

[25] T. de Rooij, R. Sitarz, O.R. Busch, M.G. Besselink, M. Abu Hilal, Technical aspects of laparoscopic distal pancreatectomy for benign and malignant disease: review of the literature, [Internet], Gastroenterol Res Pract 2015 (2015) 472906. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26240565.

[26] W. Kimura, T. Inoue, N. Futakawa, H. Shinkai, I. Han, T. Muto, Spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein, [Internet], Surgery 120 (5) (1996 Nov) 885–890. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8909526.

[27] M.A. Adam, K. Choudhury, M.A. Dinan, S.D. Reed, R.P. Scheri, D.G. Blazer, et al., Minimally invasive versus open pancreaticoduodenectomy for cancer, [Internet], Ann Surg 262 (2) (2015 Aug) 372–377. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26158612.

[28] M. Gagner, A. Pomp, Laparoscopic pancreatic resection: is it worthwhile? [Internet], J Gastrointest Surg 1 (1) (1997) 20–25 discussion 25-6. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9834326.

[29] J.A. Stauffer, A. Coppola, D. Villacreses, K. Mody, E. Johnson, Z. Li, et al., Laparoscopic versus open pancreaticoduodenectomy for pancreatic adenocarcinoma: long-term results at a single institution, Surg Endosc Other Interv Tech 31 (5) (2017) 2233–2241.

[30] S.M. Sharpe, M.S. Talamonti, C.E. Wang, R.A. Prinz, K.K. Roggin, D.J. Bentrem, 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, [Internet], J Am Coll Surg 221 (1) (2015 Jul 1) 175–184. Available from: https://www.sciencedirect.com/science/article/pii/S1072751515003361.

[31] K.P. Croome, M.B. Farnell, F.G. Que, Km Reid-Lombardo, M.J. Truty, D.M. Nagorney, et al., Total laparoscopic pancreaticoduodenectomy for pancreatic ductal adenocarcinoma, Ann Surg [Internet] 260 (4) (2014 Oct) 633–640. Available from: https://insights.ovid.com/crossref?an=00000658-201410000-00009.

[32] N.C. Buchs, P. Addeo, F.M. Bianco, S. Ayloo, E. Benedetti, P.C. Giulianotti, Robotic versus open pancreaticoduodenectomy: a comparative study at a single institution, World J Surg [Internet] 35 (12) (2011 Dec 24) 2739–2746. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21947494.

[33] H.J. Asbun, J.A. Stauffer, Laparoscopic vs Open Pancreaticoduodenectomy: Overall Outcomes and Severity of Complications Using the Accordion Severity Grading System, (2012), https://doi.org/10.1016/j.jamcollsurg.2012.08.006 Available from.

[34] S. Andrianello, G. Marchegiani, G. Malleo, V. Allegrini, A. Pulvirenti, A. Giardino, et al., Polyester sutures for pancreaticojejunostomy protect against postoperative pancreatic fistula: a case–control, risk-adjusted analysis, [Internet], HPB 20 (10) (2018 Oct) 977–983. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29853432.

[35] G. Nigri, N. Petrucciani, M. La Torre, P. Magistri, S. Valabrega, P. Aurello, et al., Duodenopancreatectomy: open or minimally invasive approach? The Surgeon 12 (4) (2014) 227–234.

[36] C. Palanivelu, P. Senthilnathan, S.C. Sabnis, N.S. Babu, S. Srivatsan Gurumurthy, N. Anand Vijai, et al., Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours, [Internet], Br J Surg 104 (11) (2017 Oct) 1443–1450, https://doi.org/10.1002/bjs.10662 Available from:.

[37] J.E. Murphy, J.Y. Wo, D.P. Ryan, W. Jiang, B.Y. Yeap, L.C. Drapek, et al., Total Neoadjuvant Therapy With FOLFIRINOX Followed by Individualized Chemoradiotherapy for Borderline Resectable Pancreatic Adenocarcinoma, [Internet], JAMA Oncol 4 (7) (2018 Jul 1) 963. Available from: http://oncology.jamanetwork.com/article.aspx?doi=10.1001/jamaoncol.2018.0329.

[38] M. Raoof, P.H.G. Ituarte, Y. Woo, S.G. Warner, G. Singh, Y. Fong, et al., Propensity score-matched comparison of oncological outcomes between laparoscopic and open distal pancreatic resection, Br. J. Surg. 105 (5) (2018) 578–586.

[39] D.-J. Yang, J.-J. Xiong, H.-M. Lu, Y. Wei, L. Zhang, S. Lu, et al., The oncological safety in minimally invasive versus open distal pancreatectomy for pancreatic ductal adenocarcinoma: a systematic review and meta-analysis, [Internet], Sci Rep 9 (1) (2019) 1159. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30718559.

[40] R.C. Langan, J.A. Graham, A.B. Chin, A.J. Rubinstein, K. Oza, J.A. Nusbaum, et al., Laparoscopic-assisted versus open pancreaticoduodenectomy: early favorable physical quality-of-life measures, [Internet], Surg (United States) 156 (2) (2014) 379–384, https://doi.org/10.1016/j.surg.2014.03.018 Available from:.

[41] C.M. Vollmer, H.J. Asbun, J. Barkun, M.G. Besselink, U. Boggi, K.C.P. Conlon, et al., Proceedings of the first international state-of-the-art conference on minimally-invasive pancreatic resection (MIPR), HPB 171–7 (2017).

[42] S. Liang, U. Hameed, S. Jayaraman, Laparoscopic pancreatectomy: indications and outcomes, [Internet], World J Gastroenterol 20 (39) (2014) 14246–14254. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4202353/pdf/WJG-20-14246.pdf.

[43] P. McCulloch, J.A. Cook, D.G. Altman, C. Heneghan, M.K. Diener, IDEAL Group, IDEAL framework for surgical innovation 1: the idea and development stages, [Internet], BMJ (2013) 346 f3012. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23778427.

[44] M. Wang, L. Meng, Y. Cai, Y. Li, X. Wang, Z. Zhang, et al., Learning curve for laparoscopic pancreaticoduodenectomy: a CUSUM analysis, J. Gastrointest. Surg. 20 (5) (2016) 924-11; Available from: https://link.springer.com/content/pdf/10.1007%2Fs11605-016-3105-3.pdf.

[45] C. Lu, W. Jin, Y.-P. Mou, J. Zhou, X. Xu, T. Xia, et al., Analysis of learning curve for laparoscopic pancreaticoduodenectomy, [Internet], J Vis Surg 2 (2016) 145. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29078532.

[46] M. Braga, C. Ridolfi, G. Balzano, R. Castoldi, N. Pecorelli, Valerio, et al., Learning curve for laparoscopic distal pancreatectomy in a high-volume hospital, Updates Surg 64 (3) (2012) 179-4; Available from: http://www.clinicaltrials.gov.

[47] I. Nachmany, N. Pencovich, A. Ben-Yehuda, G. Lahat, R. Nakache, Y. Goykhman, et al., Laparoscopic distal pancreatectomy: learning curve and experience in a tertiary center, [Internet], J Laparoendosc Adv Surg Tech 26 (6) (2016) 470–474. Available from: http://www.liebertpub.com/doi/10.1089/lap.2016.0098.

[48] C. Ricci, R. Casadei, S. Buscemi, G. Taffurelli, M. D'Ambra, C.A. Pacilio, et al., Laparoscopic distal pancreatectomy: what factors are related to the learning curve? [Internet], Surg Today 45 (1) (2015 Jan 9) 50–56. Available from: http://www.ncbi.nlm.nih.gov/pubmed/24610347.

[49] T. de Rooij, F. Cipriani, M. Rawashdeh, S. van Dieren, S. Barbaro, M. Abuawwad, et al., Single-surgeon learning curve in 111 laparoscopic distal pancreatectomies: does operative time tell the whole story? [Internet], J Am Coll Surg 224 (5) (2017) 826–832 e1. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1072751517300637.

[50] K.P. Croome, M.B. Farnell, F.G. Que, Km Reid-Lombardo, M.J. Truty, D.M. Nagorney, et al., Pancreaticoduodenectomy with major vascular resection: a comparison of laparoscopic versus open approaches, [Internet], J Gastrointest Surg 19 (1) (2015) 189–194. Available from: http://link.springer.com/10.1007/s11605-014-2644-8.

[51] G.M. Garbarino, D. Fuks, J. Cowan, M. Ward, F. Moisan, G. Donatelli, et al., Total laparoscopic pancreaticoduodenectomy with venous reconstruction for pancreatic head cancer with involvement of the superior mesenteric vein–portal vein confluence, [Internet], Ann Surg Oncol 25 (13) (2018) 4035–4036. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30218250.